```
=> d his ful

     (FILE 'HOME' ENTERED AT 16:50:24 ON 13 MAR 2006)

     FILE 'REGISTRY' ENTERED AT 16:51:22 ON 13 MAR 2006
L5              STR
L7         118852 SEA SSS FUL L5
L8              STR
L9            157 SEA SUB=L7 SSS FUL L8
L10             STR
L11            18 SEA SUB=L9 SSS FUL L10

     FILE 'HCAPLUS' ENTERED AT 16:55:16 ON 13 MAR 2006
L12             7 SEA ABB=ON  PLU=ON  L11
                  D STAT QUE
                  D IBIB ABS HITSTR L12 1-7

     FILE 'REGISTRY' ENTERED AT 16:56:25 ON 13 MAR 2006
                  D IDE CAN L11 1-18

     FILE 'BEILSTEIN' ENTERED AT 17:02:58 ON 13 MAR 2006
L13             4 SEA SSS FUL L10
L14             3 SEA ABB=ON  PLU=ON  L13 NOT L11
                  D STAT QUE L14
                  D BRN CN MF FW STR PHARM RX L14 1-3

     FILE 'HCAPLUS' ENTERED AT 17:37:44 ON 13 MAR 2006
L15            43 SEA ABB=ON  PLU=ON  ("EMIG P"/AU OR "EMIG PETER"/AU)
L16            41 SEA ABB=ON  PLU=ON  L15 NOT L12
                  D STAT QUE L16
                  D IBIB ABS L16 1-41
L17            67 SEA ABB=ON  PLU=ON  ("GUNTHER E"/AU OR "GUNTHER ECKHARD"/AU)
                  NOT (L12 OR L16)
                  D STAT QUE L17
                  D IBIB ABS L17 1-67
L18             1 SEA ABB=ON  PLU=ON  (("AUE B J"/AU OR "AUE BEATE"/AU)) NOT
                  (L12 OR L16 OR L17)
                  D STAT QUE NOS L18
                  D IBIB ABS L18 1
L19            41 SEA ABB=ON  PLU=ON  (("POLYMEROPOULOS E"/AU OR "POLYMEROPOULOS
                  E E"/AU OR "POLYMEROPOULOS EMANUELE E"/AU OR "POLYMEROPOULOS
                  EMMANUEL"/AU OR "POLYMEROPOULOS EMMANUEL E"/AU)) NOT (L12 OR
                  L16 OR L17 OR L18)
                  D STAT QUE L19 NOS
                  D IBIB ABS L19 1-41
L20            12 SEA ABB=ON  PLU=ON  (("BAASNER S"/AU OR "BAASNER SIIKE"/AU OR
                  "BAASNER SILKE"/AU)) NOT (L12 OR L16 OR L17 OR L18 OR L19)
                  D STAT QUE L20 NOS
                  D IBIB ABS L20 1-12
L21          1218 SEA ABB=ON  PLU=ON  ("SCHMIDT P"/AU OR "SCHMIDT P A"/AU OR
                  "SCHMIDT P B JR"/AU OR "SCHMIDT P C"/AU OR "SCHMIDT P D"/AU OR
                  "SCHMIDT P E"/AU OR "SCHMIDT P F"/AU OR "SCHMIDT P G"/AU OR
                  "SCHMIDT P H"/AU OR "SCHMIDT P HENRY"/AU OR "SCHMIDT P J"/AU
                  OR "SCHMIDT P K"/AU OR "SCHMIDT P K H"/AU OR "SCHMIDT P KARL
                  HEINZ"/AU OR "SCHMIDT P L"/AU OR "SCHMIDT P M"/AU OR "SCHMIDT
                  P N"/AU OR "SCHMIDT P O"/AU OR "SCHMIDT P P"/AU OR "SCHMIDT P
                  P JR"/AU OR "SCHMIDT P R"/AU OR "SCHMIDT P R L"/AU OR "SCHMIDT
                  P S"/AU OR "SCHMIDT P T"/AU OR "SCHMIDT P U"/AU OR "SCHMIDT P
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                  P WORSOE"/AU) OR SCHMIDT PETER ?/AU
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L22      100932 SEA ABB=ON  PLU=ON  L7
L23           5 SEA ABB=ON  PLU=ON  (L21 AND L22) NOT (L12 OR L16 OR L17 OR
               L18 OR L19 OR L20)
               D STAT QUE
               D IBIB ABS HITSTR L23 1-5


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   12 MAR 2006  HIGHEST RN 876514-29-3
     DICTIONARY FILE UPDATES:  12 MAR 2006  HIGHEST RN 876514-29-3

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
     ************************************************************

     Structure search iteration limits have been increased.  See HELP SLIMITS
     for details.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html

     FILE HCAPLUS

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     26, 1996), unless otherwise indicated in the original publications.
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     strictly prohibited.

     FILE COVERS 1907 - 13 Mar 2006  VOL 144 ISS 12
     FILE LAST UPDATED: 12 Mar 2006  (20060312/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.
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This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BEILSTEIN
FILE LAST UPDATED ON JANUARY 17, 2006

FILE COVERS 1771 TO 2005.
**FILE CONTAINS 9,428,406 SUBSTANCES**

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

**********
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *
**********

**NEW**

*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**

*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:55:16 ON 13 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 13 Mar 2006  VOL 144 ISS 12
FILE LAST UPDATED: 12 Mar 2006  (20060312/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L5                STR
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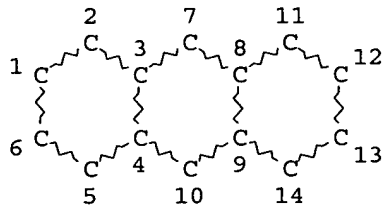


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
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L8               STR
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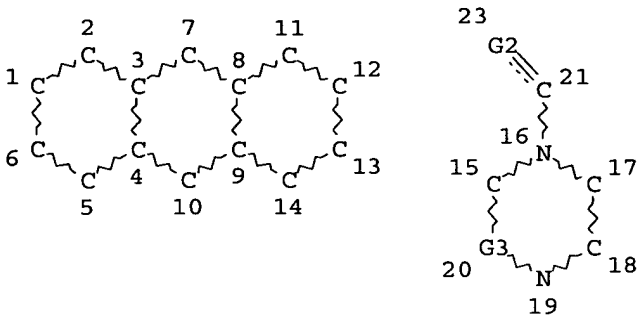

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REP G3=(1-4) C
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 16
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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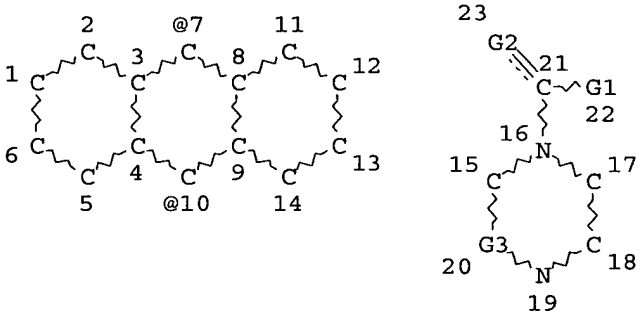
L10 STR



VAR G1=7/10
VAR G2=O/S
REP G3=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 15
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
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L12 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

=>
=>

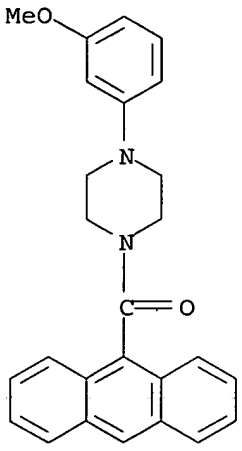
=> d ibib abs hitstr l12 1-7

L12 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:53490 HCAPLUS
DOCUMENT NUMBER: 142:309180
TITLE: Design and synthesis of a focused library of novel aryl- and heteroaryl-ketopiperazides
AUTHOR(S): Gerlach, Matthias; Claus, Eckhard; Baasner, Siike; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen
CORPORATE SOURCE: Drug Discovery, Zentaris GmbH, Frankfurt am Main, Germany
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2004), 337(12), 695-703
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1-Phenyl-4-piperazinyl-carbonyl-substituted nitrogen-containing heterocycles were discovered at Zentaris as a new class of potent, synthetic, small mol. tubulin inhibitors with strong antiproliferative activity. The lead structure of this class, D-24203, proved to be a potent inhibitor of in vivo tumor growth in different xenograft models including mammary and renal cancers. As part of our efforts in the lead optimization process to expand structural diversity as well as to optimize bioavailability parameters such as solubility and metabolic stability for these compds., we produced and evaluated a focused library containing 320 compds. Five new heterocyclic compound classes with comparable activity properties in the cytotoxicity and tubulin polymerization assay could be identified. In silico calculated bioavailability parameters for selected library members provides new compound classes with improved solubility properties. Library design, development of adequate solution phase methodol., and synthesis will be presented, as well as results of lead optimization.

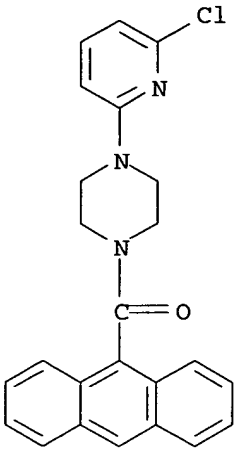
IT **848084-63-9 848084-64-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(design and synthesis of a focused library of novel aryl- and heteroaryl-ketopiperazides)

RN 848084-63-9 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)




RN 848084-64-0 HCAPLUS

CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(6-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)



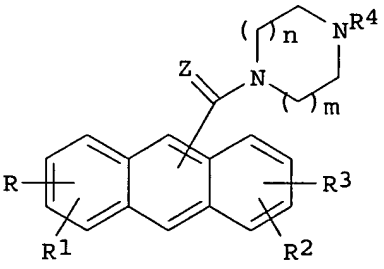
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:75996 HCAPLUS
DOCUMENT NUMBER: 140:146164
TITLE: Preparation of (anthracenyl)(piperazinyl)methanones as antitumor agents
INVENTOR(S): Emig, Peter; Guenther, Eckhard; Aue, Beate; Polymeropoulos, Emmanuel; Baasner, Silke; Schmidt, Peter
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: Ger. Offen., 31 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10232525 | A1 | 20040129 | DE 2002-10232525 | 20020718 |

PRIORITY APPLN. INFO.: DE 2002-10232525 20020718
OTHER SOURCE(S): MARPAT 140:146164
GI

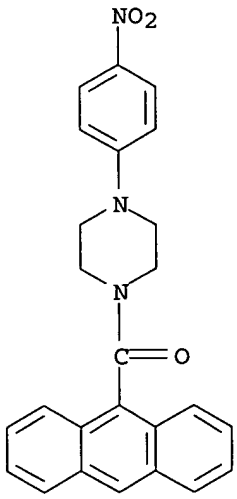


I

AB Title compds. [I; R-R3 = H, OH, halo, (branched) alkyl, cycloalkyl, alkylcarbonyl, alkoxy, arylalkoxy, etc.; Z = O, S; n, m = 0-4; R4 = (branched) (saturated) (substituted) alkyl, aryl, arylalkyl, etc.], were prepared Thus, anthracene-9-carboxylic acid in DMF was treated successively with N-methylmorpholine, 1-(4-nitrophenyl)piperazine, and Py-BOP followed by stirring for 4 h at room temperature to give 79.7% 1-(4-nitrophenyl)-4-(anthracen-9-ylcarbonyl)piperazine. Anthracen-9-yl-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]methanone inhibited proliferation of different human tumor cells in XTT cytotoxicity test with EC50 = 0.047->3.16 μg/mL.

IT **647854-29-3P 647854-30-6P 647854-31-7P**
**647854-32-8P 647854-33-9P 647854-34-0P**
**647854-35-1P 647854-36-2P 647854-37-3P**
**647854-38-4P 647854-39-5P 647854-40-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (anthracenyl)(piperazinyl)methanones as antitumor agents)

RN 647854-29-3 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)




RN 647854-30-6 HCAPLUS
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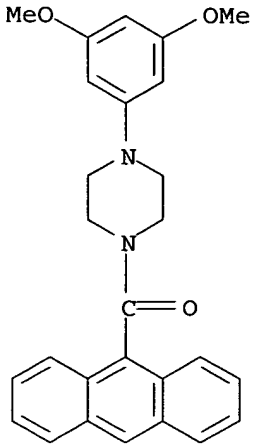
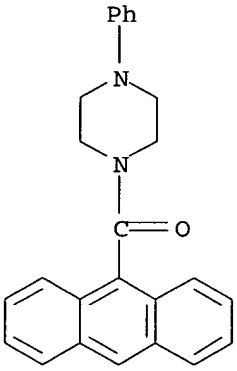



RN 647854-31-7 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-phenyl- (9CI) (CA INDEX NAME)




RN 647854-32-8 HCAPLUS
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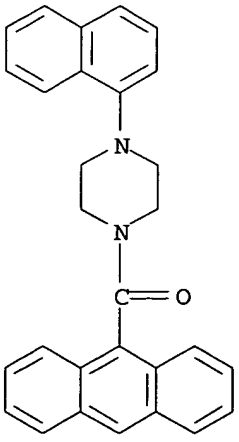

RN 647854-33-9 HCAPLUS
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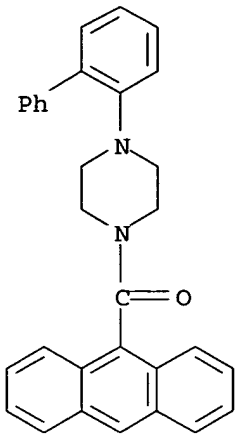
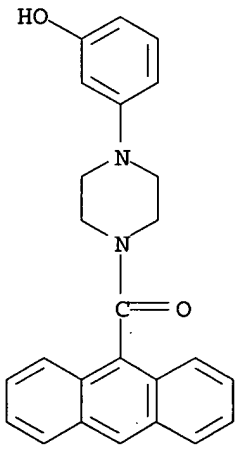



RN 647854-34-0 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)




RN 647854-35-1 HCAPLUS
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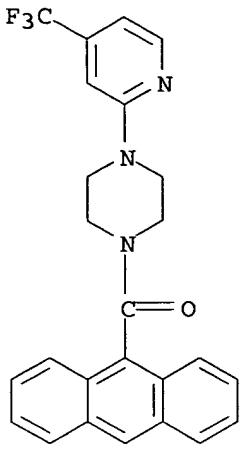
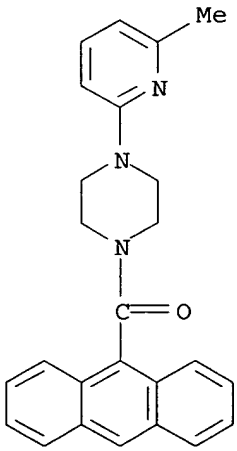


RN 647854-36-2 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)



RN 647854-37-3 HCAPLUS
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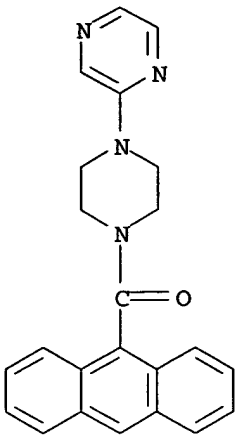

RN 647854-38-4 HCAPLUS
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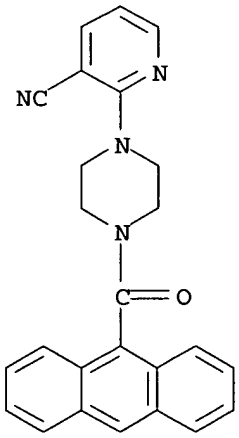

RN 647854-39-5 HCAPLUS
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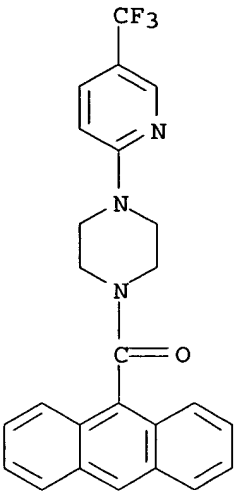

RN 647854-40-8 HCAPLUS
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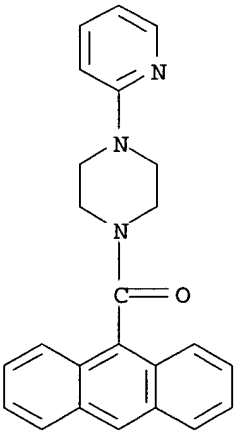


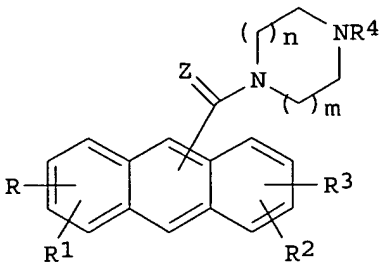
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:60486 HCAPLUS
DOCUMENT NUMBER: 140:111430
TITLE: Preparation of (anthracenyl)(piperazinyl)methanones as antitumor agents
INVENTOR(S): Emig, Peter; Guenther, Eckhard; Aue, Beate; Polymeropoulos, Emmanuel; Baasner, Silke; Schmidt, Peter
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2004007470 | A1 | 20040122 | WO 2003-EP5156 | | 20030516 |
| W: AU, BR, BY, CA, CN, CO, GE, HR, HU, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, UA, UZ, YU, ZA | | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | | | |
| AU 2003232785 | A1 | 20040202 | AU 2003-232785 | | 20030516 |
| EP 1521748 | A1 | 20050413 | EP 2003-763626 | | 20030516 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK | | | | | |
| CN 1668604 | A | 20050914 | CN 2003-816919 | | 20030516 |
| JP 2005537258 | T2 | 20051208 | JP 2004-520367 | | 20030516 |
| CA 2435399 | AA | 20040117 | CA 2003-2435399 | | 20030717 |
| US 2004110756 | A1 | 20040610 | US 2003-621590 | | 20030717 |
| PRIORITY APPLN. INFO.: | | | US 2002-396683P | P | 20020717 |
| | | | WO 2003-EP5156 | W | 20030516 |

OTHER SOURCE(S): MARPAT 140:111430
GI



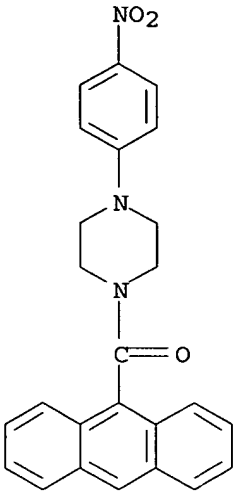

I

AB Title compds. [I; R-R3 = H, OH, halo, (branched) alkyl, cycloalkyl, alkylcarbonyl, alkoxy, arylalkoxy, etc.; Z = O, S; n, m = 0-4; R4 = (branched) (saturated) (substituted) alkyl, aryl, arylalkyl, etc.], were prepared Thus, anthracene-9-carboxylic acid in DMF was treated successively with N-methylmorpholine, 1-(4-nitrophenyl)piperazine, and Py-BOP followed by stirring for 4 h at room temperature to give 79.7% 1-(4-nitrophenyl)-4-(anthracen-9-ylcarbonyl)piperazine. Anthracen-9-yl-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]methanone inhibited proliferation of different human tumor cells in XTT cytotoxicity test with EC50 = 0.047->3.16 μg/mL.

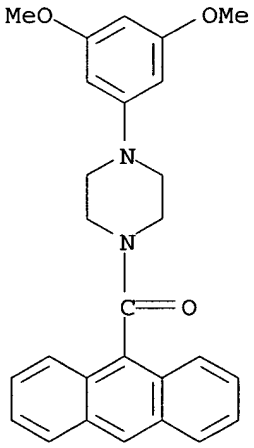
IT **647854-29-3P 647854-30-6P 647854-31-7P**
**647854-32-8P 647854-33-9P 647854-34-0P**
**647854-35-1P 647854-36-2P 647854-37-3P**
**647854-38-4P 647854-39-5P 647854-40-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (anthracenyl)(piperazinyl)methanones as antitumor agents)

RN 647854-29-3 HCAPLUS

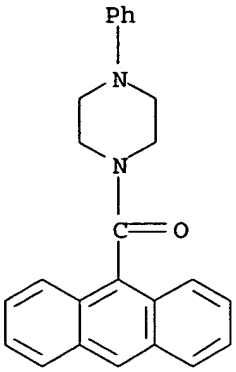
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



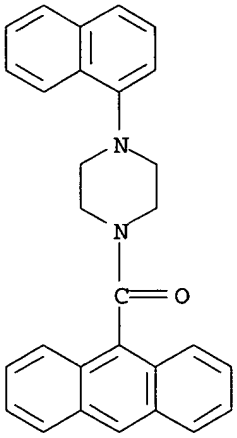

RN 647854-30-6 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



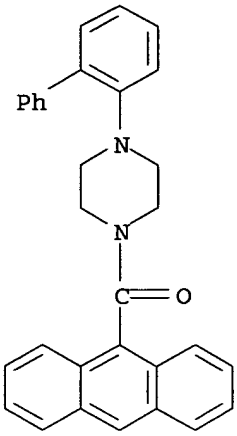

RN 647854-31-7 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-phenyl- (9CI) (CA INDEX NAME)



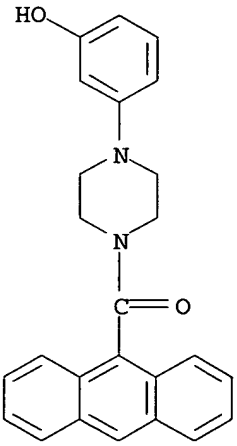
RN 647854-32-8 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(1-naphthalenyl)- (9CI) (CA INDEX NAME)



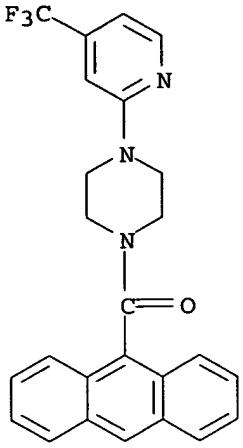
RN 647854-33-9 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-[1,1'-biphenyl]-2-yl- (9CI) (CA INDEX NAME)



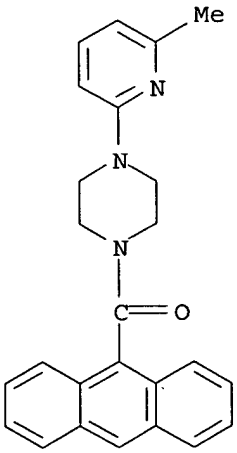

RN 647854-34-0 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)



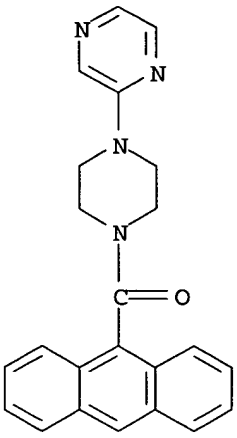

RN 647854-35-1 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-[4-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



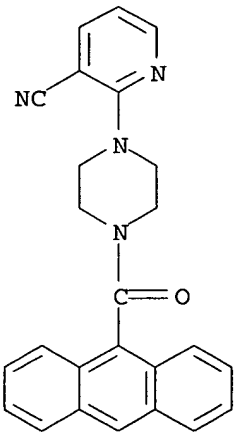
RN 647854-36-2 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)



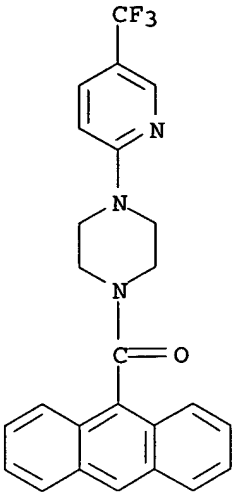
RN 647854-37-3 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-pyrazinyl- (9CI) (CA INDEX NAME)



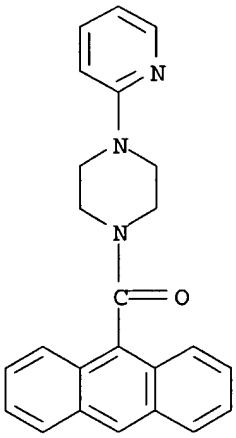
RN 647854-38-4 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-cyano-2-pyridinyl)- (9CI) (CA INDEX NAME)



RN 647854-39-5 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-[5-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 647854-40-8 HCAPLUS
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

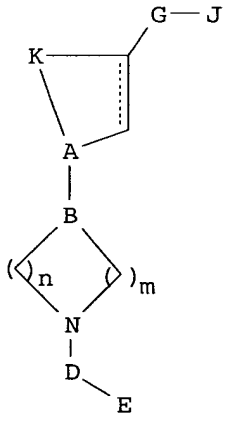
L12 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:696782 HCAPLUS
DOCUMENT NUMBER: 139:230625
TITLE: Preparation of bipiperidinyl and related compounds as acetyl CoA carboxylase inhibitors useful against metabolic syndrome and other disorders
INVENTOR(S): Perry, David Austen; Harwood, Harold James, Jr.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

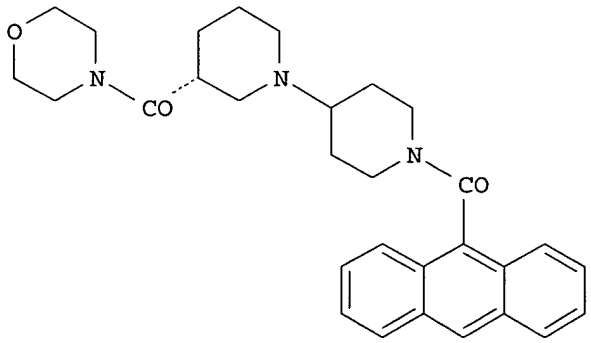
| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2003072197 | A1 | 20030904 | WO 2003-IB573 | | 20030217 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| AU 2003248354 | A1 | 20030909 | AU 2003-248354 | | 20030217 |
| EP 1478437 | A1 | 20041124 | EP 2003-742882 | | 20030217 |
| EP 1478437 | B1 | 20050831 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| AT 303178 | E | 20050915 | AT 2003-742882 | | 20030217 |
| US 2003187254 | A1 | 20031002 | US 2003-370844 | | 20030220 |
| US 6979741 | B2 | 20051227 | | | |
| NO 2004004034 | A | 20041124 | NO 2004-4034 | | 20040924 |
| PRIORITY APPLN. INFO.: | | | US 2002-365358P | P | 20020227 |
| | | | WO 2003-IB573 | W | 20030217 |

OTHER SOURCE(S): MARPAT 139:230625

GI




I




II

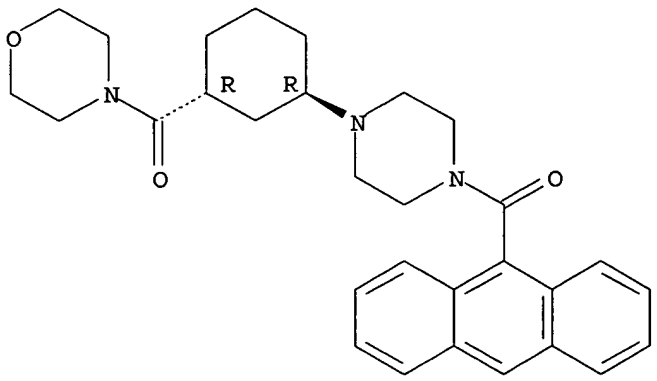
AB Acetyl CoA carboxylase (ACC) inhibitors (shown as I; variables defined below; most examples include the bipiperidinyl ring system, e.g. (anthracen-9-yl)[(3R)-3-(morpholine-4-carbonyl)[1,4']bipiperidinyl-1'-yl]methanone), pharmaceutical compns. containing such compds. and the use of such compds. to treat for example, Metabolic Syndrome, atherosclerosis, diabetes and obesity are disclosed. None of pharmacol. activity, therapeutic uses and methods of preparation is claimed and pharmacol. data are not included. More than 200 example prepns. and/or characterization data are included for I and intermediates. For I: A-B is N-CH or CH-N; K is (CH2)r (r = 2-4); m and n = 1-3 when A-B is N-CH or 2 or 3 when A-B is CH-N; the dashed line = the presence of an optional double bond; D is carbonyl or sulfonyl. E is either (a) a bicyclic ring consisting of two

fused fully unsatd. 5-7 membered rings, taken independently, each of said rings optionally having 1-4 heteroatoms = O, S and N; or (b) a tricyclic ring consisting of two fused fully unsatd. 5-7 membered rings, taken independently, each of said rings optionally having 1-4 heteroatoms = O, S and N, said two fused rings fused to a 3rd partially saturated, fully unsatd. or fully saturated 5-7 membered ring, said 3rd ring optionally having 1-4 heteroatoms = O, S and N. Or (c) a tetracyclic ring comprising a bicyclic ring consisting of two fused fully unsatd. 5-7 membered rings, taken independently, each of said rings optionally having 1-4 heteroatoms = O, S and N, said bicyclic ring fused to two fully saturated, partially saturated or fully unsatd. 5-7 membered monocyclic rings taken independently, each of said rings optionally having 1-4 heteroatoms = O, S and N or said bicyclic ring fused to a 2nd bicyclic ring consisting of two fused fully saturated, partially saturated or fully unsatd. 5-7 membered rings, taken independently, each of said rings optionally having 1-4 heteroatoms = O, S and N; or (d) a teraryl ring comprising a fully unsatd. 5-7 membered ring, said ring optionally having 1-4 heteroatoms = O, S and N, and said ring disubstituted independently with a fully unsatd. 5-7 membered ring to form a teraryl nonfused ring system, each of said substituent rings optionally having 1-4 heteroatoms = O, S and N. G is carbonyl, sulfonyl or CR7R8 (R7 and R8 = H, (C1-C6)alkyl, (C2-C6) alkenyl or (C2-C6)alkynyl or a 5-7 membered partially saturated, fully saturated or fully unsatd. ring optionally having one heteroatom = O, S and N); J is OR1, NR2R3 or CR4R5R6; addnl. details including provisos are given in the claims.

IT **591781-15-6P**, (Anthracen-9-yl)[4-[(1R,3R)-3-[(morpholin-4-yl)carbonyl]cyclohexyl]piperazin-1-yl]methanone **591781-16-7P**, (Anthracen-9-yl)[4-[(1S,3R)-3-[(morpholin-4-yl)carbonyl]cyclohexyl]piperazin-1-yl]methanone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of bipiperidinyl and related compds. as acetyl CoA carboxylase inhibitors useful against metabolic syndrome and other disorders)

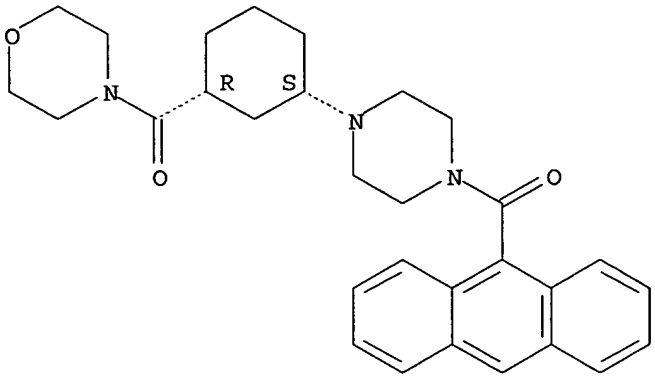
RN 591781-15-6 HCAPLUS
CN Morpholine, 4-[[(1R,3R)-3-[4-(9-anthracenylcarbonyl)-1-piperazinyl]cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 591781-16-7 HCAPLUS
CN Morpholine, 4-[[(1R,3S)-3-[4-(9-anthracenylcarbonyl)-1-piperazinyl]cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



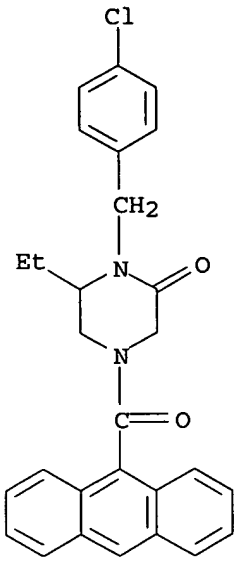
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:641466 HCAPLUS
DOCUMENT NUMBER: 133:350193
TITLE: Non-amide-based combinatorial libraries derived from N-BOC-iminodiacetic acid: solution-phase synthesis of piperazinone libraries with activity against LEF-1/β-catenin-mediated transcription
AUTHOR(S): Boger, Dale L.; Goldberg, Joel; Satoh, Shigeki; Ambroise, Yves; Cohen, Steven B.; Vogt, Peter K.
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Helvetica Chimica Acta (2000), 83(8), 1825-1845
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of a solution-phase approach to the rapid, parallel synthesis of highly functionalized piperazinones in only four steps starting from N-BOC-iminodiacetic acid is detailed. The efforts represent the extension of the solution-phase synthesis of combinatorial libraries from N-BOC-iminodiacetic acid to non-amide-based libraries where simple liquid-liquid extns. are employed to purify all reaction products. This methodol. was applied to the synthesis of a diverse 150-member library with substituents in three positions of the piperazinone core. Screening results from a luciferase reporter assay indicate that a number of library members are novel repressors of LEF-1/β-catenin-mediated transcription, and may be effective agents against colorectal tumors. Two secondary libraries (100 members each) designed from these lead structures were synthesized and screened, providing addnl. active agents and insight into key structure-activity relationships in the series. These compds. represent only the second class of small mols. which repress transcription of reporter genes containing LEF-1 responsive elements, and the first group not based on DNA minor-groove-binding agents.

IT **305327-53-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of non-amide-based combinatorial libraries derived from N-BOC-iminodiacetic acid and solution-phase synthesis of piperazinone libraries with activity against lymphoid-enhancer factor-1/β-

catenin-mediated transcription)
RN 305327-53-1 HCAPLUS
CN Piperazinone, 4-(9-anthracenylcarbonyl)-1-[(4-chlorophenyl)methyl]-6-ethyl- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:501882 HCAPLUS
DOCUMENT NUMBER: 71:101882
TITLE: 9-(4-Methylpiperazino)methyl-9,10-dihydroanthracene and similar compounds active on the central nervous system
PATENT ASSIGNEE(S): Societe des usines chimiques de Rhone-Poulenc
SOURCE: Fr. M., 3 pp.
CODEN: FMXXAJ
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 5432 | | 19671113 | FR | 19660404 |

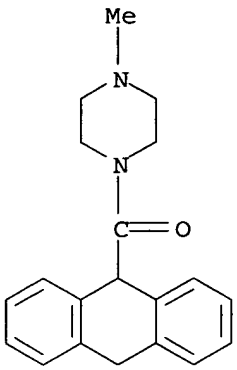
GI For diagram(s), see printed CA Issue.
AB I (R = 4-methyl-1-piperazinyl) is prepared by the reduction of 9-[(4-methyl-1-piperazinyl) carbonyl]-9,10-dihydroanthracene (II) with LiAlH4. I (R = 4-methyl-1-piperazinyl)(m. 94-5°),I(R = NH2) (m. 92-3°, HCl salt m. 285-90°,allotropic form m. 76-7° with HCl salt m. 280-5°),I(R = Me2N)(HCl salt m. 230-240°),and I(R = 4-benzyl-1-piperazinyl)(m. 116°) are useful (adult dosage 5-200 mg./day) as tranquilizers, antidepressants, anticonvulsants, anti-Parkinsonians, antihistamines, and antiserotonins. Thus, a suspension of 0.8 g. LiAlH4 in 60 ml. Et2O was treated slowly with 2.15 g. II, refluxed 2 hrs., cooled, and treated slowly with H2O 0.95, 5N soda solution 0.7, and H2O 3.1 ml. to give 1.47 g. I (R =

4-methyl-1-piperazinyl).

IT **22063-98-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 22063-98-5 HCAPLUS

CN Piperazine, 1-(9,10-dihydro-9-anthroyl)-4-methyl- (8CI) (CA INDEX NAME)




L12 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1969:37552 HCAPLUS

DOCUMENT NUMBER: 70:37552

TITLE: Anthracene derivatives

INVENTOR(S): Fouche, Jean C. L.

PATENT ASSIGNEE(S): Societe des usines chimiques de Rhone-Poulenc

SOURCE: Fr., 5 pp.
CODEN: FRXXAK

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 1505351 | | 19671215 | FR | 19660106 |

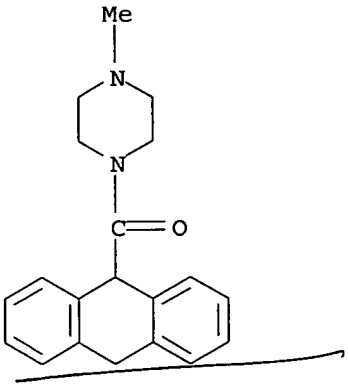
OTHER SOURCE(S): MARPAT 70:37552

GI For diagram(s), see printed CA Issue.

AB Novel derivs. (I) of 9,10-dihydroanthracene are prepared Thus, 68.5 g. LiAlH4 in 1 l. anhydrous tetrahydrofuran was treated with 133.8 g. 10-hydroximinodibenzo[a,d]cycloheptadiene in 1.2 l. tetrahydrofuran in 25 min. with rise of temperature from 25 to 60° and the mixture refluxed 8 hrs., the cooled solution (ice bath) treated successively with 90.5 ml. H2O, 59 ml. 5N NaOH, and 264 ml. H2O; the residue on filtration washed with 2.5 l. tetrahydrofuran and 700 ml. CH2Cl2, the oily residue on evaporation taken up in 700 ml. Et2O; extracted with 650 ml. aqueous 2N MeSO3H, the acid solution washed with 400 ml. Et2O, made alkaline with 180 ml. 10N NaOH, the oily product extracted with 900 ml. Et2O, washed to neutrality with 1.6 l. H2O, the dried extract evaporated, the oily residue (68 g.) taken up in 200 ml. absolute alc., treated with 78 ml. dry HCl-absolute alc. (4.2 moles HCl/l. EtOH), and cooled 2 hrs. at 5° to give 57.3 g. I.HCl (Z = CH2NH2), m. 285-90°; free base (II) m. 92-3° or 76-8°. II was also prepared from I (Z = tosyloxymethyl) and NH3. Treatment of II with HCHO and HCO2H gave I.HCl (Z = Me2NCH2), m. 230-40°, also prepared by LiAlH4 reduction of I (Z =

Me2NCO), m. 128-30°. LiAlH4 reduction of I (Z = 4-methylpiperazinocarbonyl), m. 143-5°, gave I (Z = 4-methylpiperazinomethyl), m. 94-5°, also prepared from I. HCl (Z = CH2NH2) and (ClCH2CH2)2NMe·HCl. Similarly was prepared I (Z = 4-benzylpiperazinomethyl), m. 116°. I act as tranquilizers, antidepressants, anticonvulsants, antiparkinson agents, antihistaminic, and antiserotonin remedies. They are nontoxic as bases, salts, or quaternary ammonium compds. in the doses employed.

IT **22063-98-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 22063-98-5 HCAPLUS
CN Piperazine, 1-(9,10-dihydro-9-anthroyl)-4-methyl- (8CI) (CA INDEX NAME)

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DICTIONARY FILE UPDATES: 12 MAR 2006 HIGHEST RN 876514-29-3

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* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
**********

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

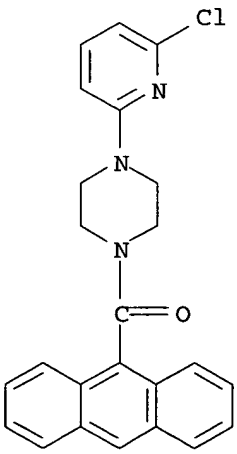
http://www.cas.org/ONLINE/UG/regprops.html

=>
=>

=> => d ide can l12 1-7
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:end

=> d ide can l11 1-18

L11 ANSWER 1 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 848084-64-0 REGISTRY
ED Entered STN: 07 Apr 2005
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(6-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H20 Cl N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



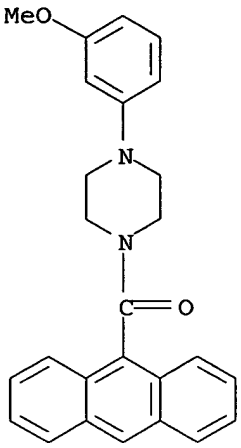

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:309180

L11 ANSWER 2 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 848084-63-9 REGISTRY
ED Entered STN: 07 Apr 2005
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C26 H24 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

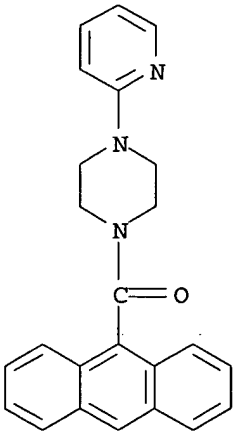



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:309180

L11 ANSWER 3 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-40-8 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H21 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



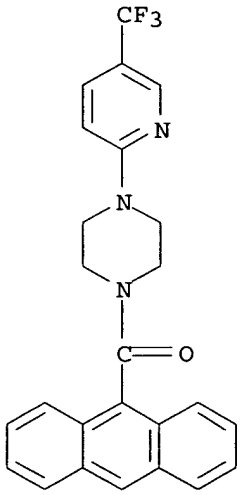
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 4 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-39-5 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-[5-(trifluoromethyl)-2-pyridinyl]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H20 F3 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

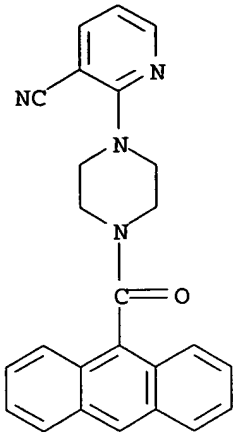
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 5 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-38-4 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-cyano-2-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H20 N4 O
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



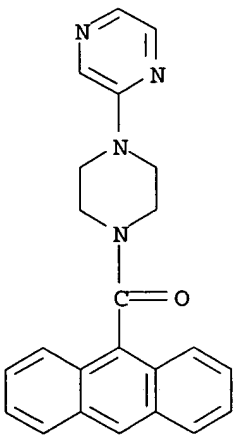
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 6 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-37-3 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-pyrazinyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H20 N4 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



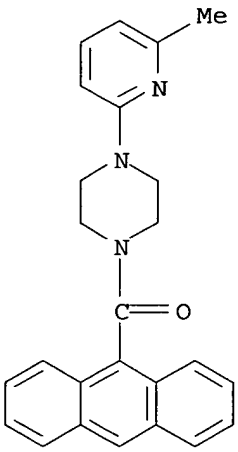
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 7 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-36-2 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H23 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



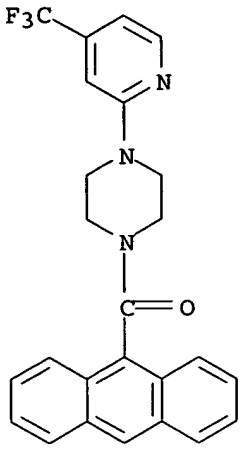

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 8 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-35-1 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-[4-(trifluoromethyl)-2-pyridinyl]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H20 F3 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



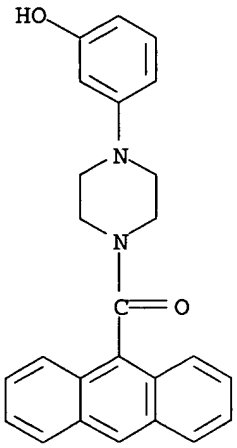
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 9 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-34-0 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



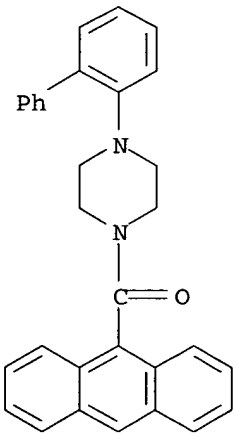
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 10 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-33-9 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-[1,1'-biphenyl]-2-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H26 N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



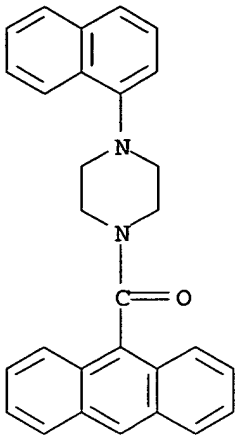

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 11 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-32-8 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(1-naphthalenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H24 N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



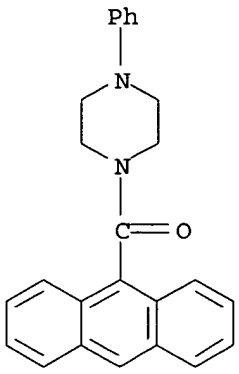
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 12 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-31-7 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-phenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



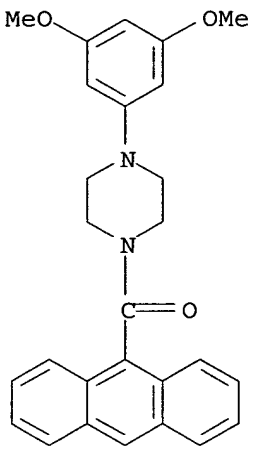
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 13 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-30-6 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H26 N2 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



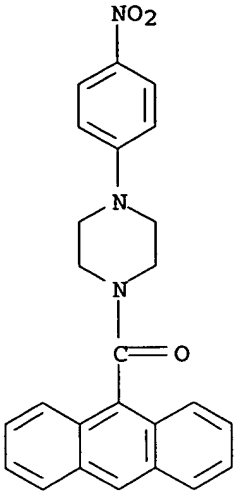

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 14 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 647854-29-3 REGISTRY
ED Entered STN: 09 Feb 2004
CN Piperazine, 1-(9-anthracenylcarbonyl)-4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H21 N3 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

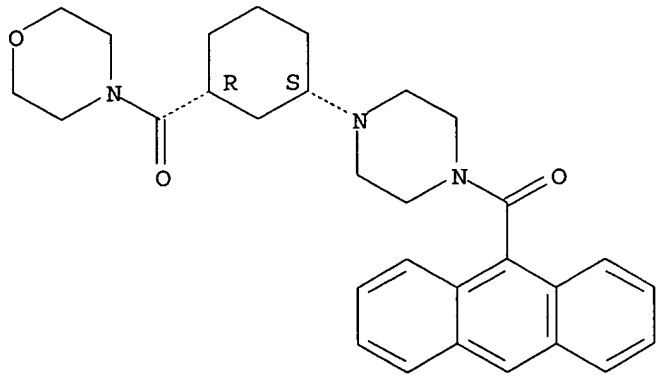
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:146164

REFERENCE 2: 140:111430

L11 ANSWER 15 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 591781-16-7 REGISTRY
ED Entered STN: 24 Sep 2003
CN Morpholine, 4-[[(1R,3S)-3-[4-(9-anthracenylcarbonyl)-1-piperazinyl]cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (Anthracen-9-yl)[4-[(1S,3R)-3-[(morpholin-4-yl)carbonyl]cyclohexyl]piperazin-1-yl]methanone
FS STEREOSEARCH
MF C30 H35 N3 O3
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



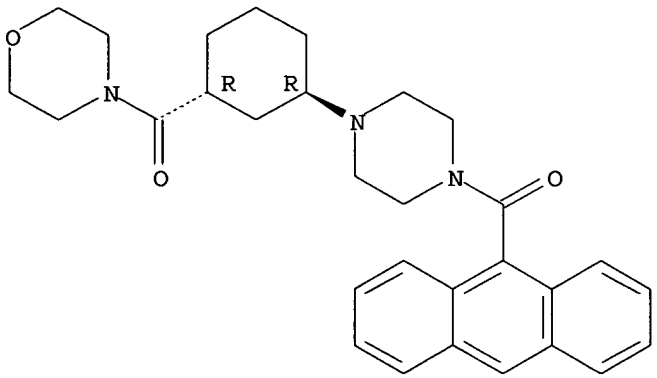
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:230625

L11 ANSWER 16 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 591781-15-6 REGISTRY
ED Entered STN: 24 Sep 2003
CN Morpholine, 4-[[(1R,3R)-3-[4-(9-anthracenylcarbonyl)-1-piperazinyl]cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (Anthracen-9-yl)[4-[(1R,3R)-3-[(morpholin-4-yl)carbonyl]cyclohexyl]piperazin-1-yl]methanone
FS STEREOSEARCH
MF C30 H35 N3 O3
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

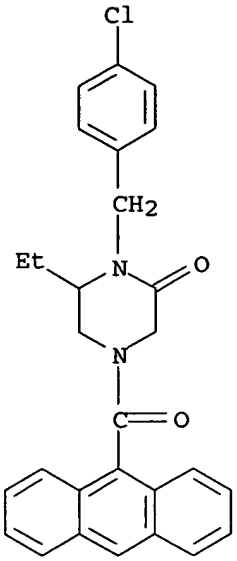



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:230625

L11 ANSWER 17 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 305327-53-1 REGISTRY
ED Entered STN: 30 Nov 2000
CN Piperazinone, 4-(9-anthracenylcarbonyl)-1-[(4-chlorophenyl)methyl]-6-ethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H25 Cl N2 O2
SR CA
LC STN Files: CA, CAPLUS

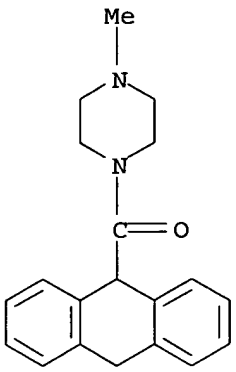



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:350193

L11 ANSWER 18 OF 18 REGISTRY COPYRIGHT 2006 ACS on STN
RN 22063-98-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN Piperazine, 1-(9,10-dihydro-9-anthroyl)-4-methyl- (8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H22 N2 O
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 71:101882

REFERENCE 2: 70:37552

=> => fil beil
FILE 'BEILSTEIN' ENTERED AT 17:02:58 ON 13 MAR 2006


FILE LAST UPDATED ON JANUARY 17, 2006

FILE COVERS 1771 TO 2005.
*** FILE CONTAINS 9,428,406 SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in
separate documents and can not be searched together in one query.
Reaction data for BEILSTEIN compounds may be displayed
immediately with the display codes PRE (preparations) and REA
(reactions). A substance answer set retrieved after the search
for a chemical name, a compounds with available reaction
information by combining with PRE/FA, REA/FA or more generally
with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
between a BEILSTEIN compound and belonging reactions. For mo
detailed reaction searches BRNs can be searched as reaction
partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

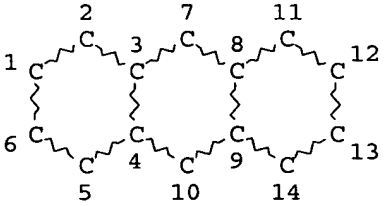
**********
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *
**********

**NEW**

*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**

*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

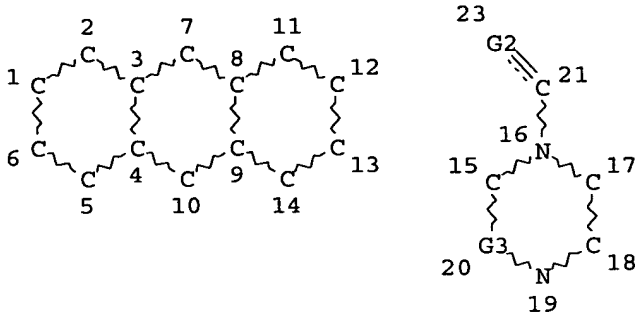
=>
=>
=> d stat que l14
L5 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 14

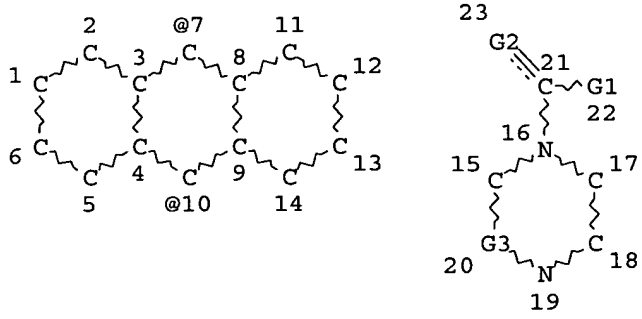
STEREO ATTRIBUTES: NONE
L7 118852 SEA FILE=REGISTRY SSS FUL L5
L8 STR




VAR G2=O/S
REP G3=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 16
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L9 157 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L10 STR




VAR G1=7/10
VAR G2=O/S
REP G3=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 15
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
L11 18 SEA FILE=REGISTRY SUB=L9 SSS FUL L10

```
L13           4 SEA FILE=BEILSTEIN SSS FUL L10
L14           3 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L13 NOT L11


=>
=> d brn cn mf fw str pharm rx l14 1-3


L14  ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

     Beilstein Records (BRN):        10031190
     Chemical Name (CN):             anthracen-9-yl-<4-(3-methoxy-phenyl)-
                                     piperazin-1-yl>-methanone
     Autonom Name (AUN):             anthracen-9-yl-<4-(3-methoxy-phenyl)-
                                     piperazin-1-yl>-methanone
     Molecular Formula (MF):         C26 H24 N2 O2
     Molecular Weight (MW):          396.49
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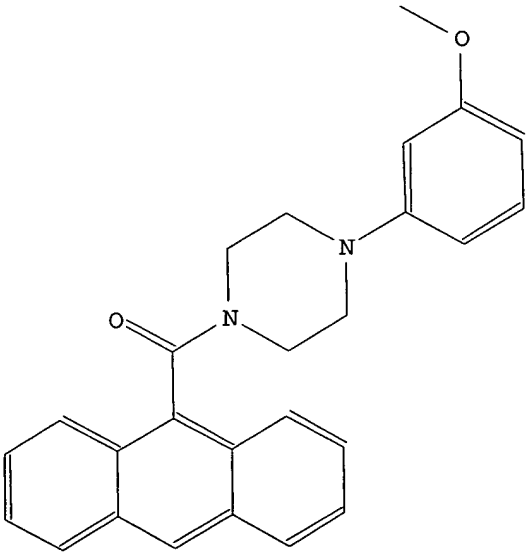



```
Pharmacological Data:
PHARM
     Effect (.E):                    cytotoxicity
     Species or Test-System (.SP):   murine leukemia L1210 cells
     Kind of Dosing (.KD):           title comp. dissolved in DMSO added
     Method, Remarks (.MR):          cells and title comp. incubated for 48 h;
                                     XTT assay used to determine proliferation;
                                     IC50-values obtained by nonlinear
                                     regression
     Further Details (.FD):          XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-
                                     3,4-tetrazolium>-bis(4-methoxy-6-
                                     nitro)benzene sulfonic acid hydrate;
                                     reference comp. paclitaxel, vincristine:
                                     IC50 = 0.06, 0.02 .my.mol/l, respectively
     Type (.TYP):                    IC50
     Value of Type (.V):             0.48 .my.mol/l
```

Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | murine leukemia P388 cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, vincristine: IC50 = 0.04, 0.004 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 0.28 .my.mol/l |

Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | murine leukemia P388ADR cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | ADR resistant cells used; XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, vincristine: IC50 = >5, 0.93 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 0.25 .my.mol/l |

Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | murine leukemia L1210VCR cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | VCR resistant cells used; XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel and vincristine: IC50 > 5 .my.mol/l, respectively |

Type (.TYP): IC50
Value of Type (.V): 0.37 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): cytotoxicity
Species or Test-System (.SP): rat leukemia LT12MDR subline cells
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression
Further Details (.FD): multi drug resistant cells used; XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, vincristine: IC50 = 0.4, 0.134 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 0.26 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): cytotoxicity
Species or Test-System (.SP): rat leukemia LT12 cells
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression
Further Details (.FD): XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, vincristine: IC50 = 0.01, 0.002 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 0.32 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): protein binding
Species or Test-System (.SP): biotin-labeled tubulin
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): diluted title comp. and <3H>colchicine transferred to a 96-well isoplate, incubated with buffer and tubulin; streptavidin-coated yttrium SPA beads added; bound radioactivity determined using scintillation counter; IC50 obtained by nonlinear regression
Further Details (.FD): reconstituted biotin-labeled tubulin

(T333, Cytoskeleton) used for <3H>colchicine competition assay; reference comp. colchicine: IC50 = 1.26 .my.mol/ml

Type (.TYP): IC50
Value of Type (.V): 4.51 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): protein polymerisation; inhibition of
Species or Test-System (.SP): bovine brain tubulin
Kind of Dosing (.KD): title comp. dissolved in DMSO
Method, Remarks (.MR): tubulin heterodimers incubated with title comp. in 96-well half area plates; tubulin polymerization determined at 340 nm; inhib. calculated from areas under the curves
Further Details (.FD): lyophilized bovine brain tubulin (2 mg/ml ML113-MAP rich or 5 mg/ml TL238-MAP free) used; MAP: microtubule associated proteine; reference comp. paclitaxel, colchicine: IC50 = >10, 2.6 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 5.59 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): cytotoxicity
Species or Test-System (.SP): non-small cell lung cancer NCI-H460 cells
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression
Further Details (.FD): XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.07 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 0.26 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): cytotoxicity
Species or Test-System (.SP): CNS cancer (glioma) SF268 cells
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear

regression
Further Details (.FD): XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.05 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 0.15 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): cytotoxicity
Species or Test-System (.SP): human ovarian carcinoma SKOV3 cells
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression
Further Details (.FD): XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.05 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 0.13 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM
Effect (.E): cytotoxicity
Species or Test-System (.SP): human cervix carcinoma KB/HeLa cells
Kind of Dosing (.KD): title comp. dissolved in DMSO added
Method, Remarks (.MR): cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression
Further Details (.FD): XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.03 .my.mol/l, respectively
Type (.TYP): IC50
Value of Type (.V): 0.14 .my.mol/l
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

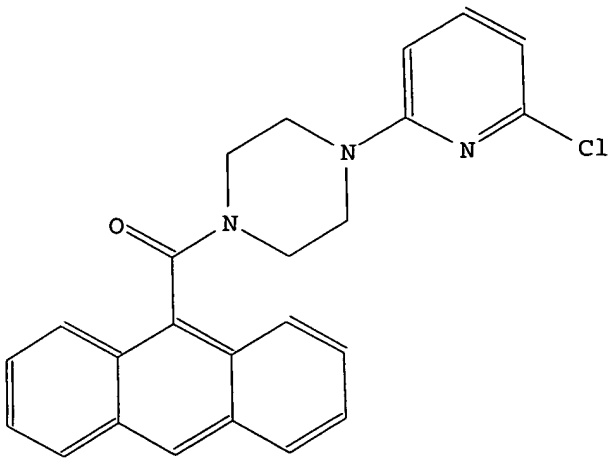
Reaction:
RX
Reaction ID (.ID): 9894343
Reactant BRN (.RBRN): 1875336, 611157
Reactant (.RCT): anthracene-9-carboxylic acid, 1-(3-methoxy-phenyl)-piperazine

Product BRN (.PBRN): 10031190
Product (.PRO): anthracen-9-yl-<4-(3-methoxy-phenyl)-piperazin-1-yl>-methanone
No. of React. Details (.NVAR): 1

Reaction Details:
RX
Reaction RID (.RID): 9894343.1
Reaction Classification (.CL): Multistage
Yield (.YDT): 9 percent (BRN=10031190)
Nr. of Stages (.SNR): 2
Stage 1
Reagent (.RGT): N-cyclohexylcarbodiimide bound to N'-methyl polystyrene HL
Solvent (.SOL): CH2Cl2
Time (.TIM): 30 min
Temperature (.T): 20 Cel
Stage 2
Stage reactant (.SRCT): 1-(3-methoxy-phenyl)-piperazine
Stage Reactant BRN (.SRBRN): 611157
Solvent (.SOL): CH2Cl2
Time (.TIM): 16 hour(s)
Temperature (.T): 20 Cel
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

L14 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN): 10030053
Chemical Name (CN): anthracen-9-yl-<4-(6-chloro-pyridin-2-yl)-piperazin-1-yl>-methanone
Autonom Name (AUN): anthracen-9-yl-<4-(6-chloro-pyridin-2-yl)-piperazin-1-yl>-methanone
Molecular Formula (MF): C24 H20 Cl N3 O
Molecular Weight (MW): 401.89



Pharmacological Data:

PHARM

| | |
|---|---|
| Effect (.E): | protein polymerisation; inhibition of |
| Species or Test-System (.SP): | bovine brain tubulin |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | tubulin heterodimers incubated with title comp. in 96-well half area plates; tubulin polymerization determined at 340 nm; inhib. calculated from areas under the curves |
| Further Details (.FD): | lyophilized bovine brain tubulin (2 mg/ml ML113-MAP rich or 5 mg/ml TL238-MAP free) used; MAP: microtubule associated proteine; reference comp. paclitaxel, colchicine: IC50 = >10, 2.6 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 6.65 .my.mol/l |

Reference(s):

1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | non-small cell lung cancer NCI-H460 cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.07 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 0.7 .my.mol/l |

Reference(s):

1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | CNS cancer (glioma) SF268 cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.05 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 0.74 .my.mol/l |

Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | human ovarian carcinoma SKOV3 cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.05 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 0.66 .my.mol/l |

Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

PHARM

| | |
|---|---|
| Effect (.E): | cytotoxicity |
| Species or Test-System (.SP): | human cervix carcinoma KB/HeLa cells |
| Kind of Dosing (.KD): | title comp. dissolved in DMSO added |
| Method, Remarks (.MR): | cells and title comp. incubated for 48 h; XTT assay used to determine proliferation; IC50-values obtained by nonlinear regression |
| Further Details (.FD): | XTT: sodium 3'-<1-(phenyl-amino-carbonyl)-3,4-tetrazolium>-bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate; reference comp. paclitaxel, colchicine: IC50 = 0.01, 0.03 .my.mol/l, respectively |
| Type (.TYP): | IC50 |
| Value of Type (.V): | 1.14 .my.mol/l |

Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

Reaction:

RX

| | |
|---|---|
| Reaction ID (.ID): | 9898858 |
| Reactant BRN (.RBRN): | 1875336, 783165 |
| Reactant (.RCT): | anthracene-9-carboxylic acid, 1-(6-chloro-pyridin-2-yl)-piperazine |
| Product BRN (.PBRN): | 10030053 |
| Product (.PRO): | anthracen-9-yl-<4-(6-chloro-pyridin-2-yl)-piperazin-1-yl>-methanone |
| No. of React. Details (.NVAR): | 1 |

Reaction Details:

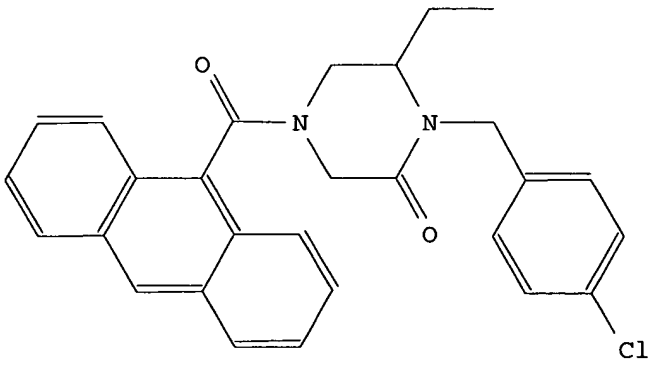
RX

| | |
|---|---|
| Reaction RID (.RID): | 9898858.1 |

Reaction Classification (.CL): Multistage
Yield (.YDT): 11 percent (BRN=10030053)
Nr. of Stages (.SNR): 2
Stage 1
Reagent (.RGT): N-cyclohexylcarbodiimide bound to N'-methyl polystyrene HL
Solvent (.SOL): CH2Cl2
Time (.TIM): 30 min
Temperature (.T): 20 Cel
Stage 2
Stage reactant (.SRCT): 1-(6-chloro-pyridin-2-yl)-piperazine
Stage Reactant BRN (.SRBRN): 783165
Solvent (.SOL): CH2Cl2
Time (.TIM): 16 hour(s)
Temperature (.T): 20 Cel
Reference(s):
1. Gerlach, Matthias; Claus, Eckhard; Baasner, Silke; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen, Arch. Pharm. (Weinheim Ger.), CODEN: ARPMAS, 337(12), <2004>, 695 - 703; BABS-6492751

L14 ANSWER 3 OF 3 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN): 8730424
Chemical Name (CN): 4-(anthracene-9-carbonyl)-1-(4-chloro-benzyl)-6-ethyl-piperazin-2-one
Autonom Name (AUN): 4-(anthracene-9-carbonyl)-1-(4-chloro-benzyl)-6-ethyl-piperazin-2-one
Molecular Formula (MF): C28 H25 Cl N2 O2
Molecular Weight (MW): 456.97




Pharmacological Data:
PHARM
Effect (.E): inhibition of gene transcription
Species or Test-System (.SP): colon-cancer cell line (SW480)
Concentration (.C): 10 .my.mol/l
Method, Remarks (.MR): cells transfected with DNA (TOPFLASH 6 .my.g); after 24 h treated with title comp.; after 48 h determined repression of LEF-1/β-catenin-mediated transcription in luciferase promoter region (TOPFLASH) by measuring luciferase

activity (luminescence)
Further Details (.FD): TOPFLASH contains four copies of the LEF-1 (lymphoid-enhancer binding factor) binding site (CCTTTGATC) upstream from the promoter that augment transcription
Results (.RE): < 1.2-fold repression of transcription
Reference(s):
1. Boger, Dale L.; Goldberg, Joel; Satoh, Shigeki; Ambroise, Yves; Cohen, Steven B.; Vogt, Peter K., Helv.Chim.Acta, CODEN: HCACAV, 83(8), <2000>, 1825 - 1845; BABS-6258794

Reaction:
RX
Reaction ID (.ID): 8678222
Reactant BRN (.RBRN): 8692887, 1875336
Reactant (.RCT): 1-(4-chloro-benzyl)-6-ethyl-piperazin-2-one, anthracene-9-carboxylic acid
Product BRN (.PBRN): 8730424
Product (.PRO): 4-(anthracene-9-carbonyl)-1-(4-chloro-benzyl)-6-ethyl-piperazin-2-one
No. of React. Details (.NVAR): 1

Reaction Details:
RX
Reaction RID (.RID): 8678222.1
Reaction Classification (.CL): Preparation
Reagent (.RGT): EtN(i-Pr)2, EDCI
Reaction Type (.TYP): Acylation
Reference(s):
1. Boger, Dale L.; Goldberg, Joel; Satoh, Shigeki; Ambroise, Yves; Cohen, Steven B.; Vogt, Peter K., Helv.Chim.Acta, CODEN: HCACAV, 83(8), <2000>, 1825 - 1845; BABS-6258794

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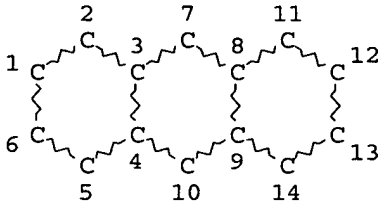


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
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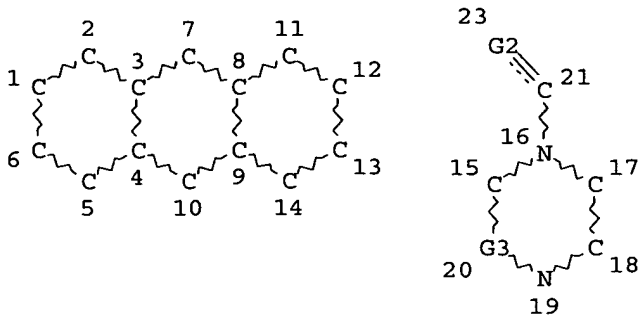
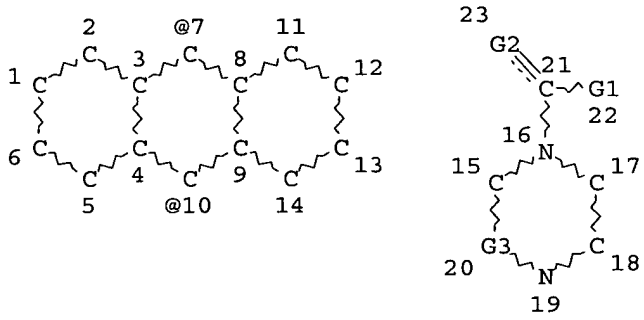
L8 STR



VAR G2=O/S
REP G3=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 16
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L9 157 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L10 STR



VAR G1=7/10
VAR G2=O/S
REP G3=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 15
NUMBER OF NODES IS 23

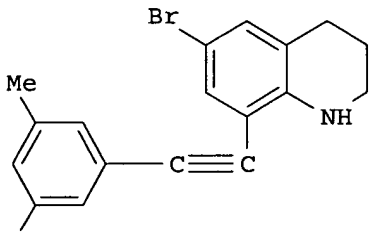
STEREO ATTRIBUTES: NONE
L11 18 SEA FILE=REGISTRY SUB=L9 SSS FUL L10
L12 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L15 43 SEA FILE=HCAPLUS ABB=ON PLU=ON ("EMIG P"/AU OR "EMIG PETER"/AU)
L16 41 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 NOT L12

=>

=>

=> d ibib abs l16 1-41

L16 ANSWER 1 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:348098 HCAPLUS
DOCUMENT NUMBER: 143:26477
TITLE: Palladium(II)-catalyzed heterocyclization of 8-arylethynyl-1,2,3,4-tetrahydroquinolines: A facile route to 2-aryl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline derivatives
AUTHOR(S): Marchand, Pascal; Puget, Alain; Le Baut, Guillaume; **Emig, Peter**; Czech, Michael; Guenther, Eckhard
CORPORATE SOURCE: Laboratoires de Chimie Organique et de Chimie Therapeutique, UPRES EA 1155, Faculte de Pharmacie, Nantes, F-44035, Fr.
SOURCE: Tetrahedron (2005), 61(16), 4035-4041
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

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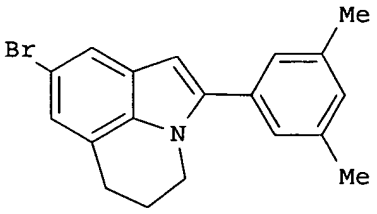



II

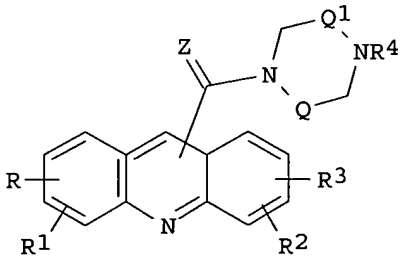
AB Dihydropyrroloquinolines have been synthesized reacting 8-arylethynyl-1,2,3,4-tetrahydroquinolines in the presence of palladium(II) chloride catalyst. Heteroannulation has been achieved in good yields and tolerates substituents on the tetrahydroquinoline, including bromo, cyano, and ester. E.g., PdCl2 catalyzed the heterocyclization of 8-arylethynyl-1,2,3,4-tetrahydroquinoline I to give 2-aryl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline II.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:74111 HCAPLUS

DOCUMENT NUMBER: 142:176867
TITLE: Preparation of acridinyl piperazinyl methanones and related compounds as anticancer drugs.
INVENTOR(S): Gerlach, Matthias; **Emig, Peter**; Paulini, Klaus; Czech, Michael; Schuster, Tilmann; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005007643 | A1 | 20050127 | WO 2004-EP7020 | 20040629 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10331500 | A1 | 20050224 | DE 2003-10331500 | 20030711 |
| PRIORITY APPLN. INFO.: | | | DE 2003-10331500 A | 20030711 |

OTHER SOURCE(S): MARPAT 142:176867
GI




I

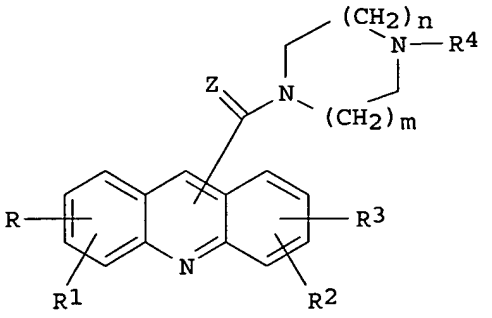
AB Title compds. [I; Z = O, S; m, n = 0-4; R-R3 = H, OH, OR5; R4 = (substituted) aryl, aralkyl, heteroaryl, heteroaralkyl; R5 = acyl; Q = (CH2)m; Q1 = (CH2)n], were prepared Thus, glutaric acid mono-[3-[4-(acridin-9-carbonyl)piperazin-1-yl]phenyl]ester showed EC50 = 0.01 μg/mL against KB/HeLa cells in an XTT proliferation assay.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:34599 HCAPLUS
DOCUMENT NUMBER: 142:134620
TITLE: Preparation of acridine derivatives as antitumor agents
INVENTOR(S): Gerlach, Matthias; **Emig, Peter**; Paulini,

Klaus; Czech, Michael; Schuster, Tilman; Gunther, Eckhard
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2005009809 | A1 | 20050113 | US 2004-879280 | | 20040629 |
| PRIORITY APPLN. INFO.: | | | US 2003-486525P | P | 20030711 |

OTHER SOURCE(S): MARPAT 142:134620
GI



I

AB The invention relates to (heterocyclylcarbonyl)acridine derivs. of the formula (I) [Z = O, S; n, m = 0-4; R, R1, R2, R3 may optionally be attached to the heteroarom. carbon atoms C1 to C9 of the acridine, are identical or different and independently of one another are H, HO or OR5, but the radicals R, R1, R2 and R3 are not simultaneously H; R4 = C6-14 aryl, C6-14 aryl-C1-4 alkyl, C2-10 heteroaryl or C2-10 heteroaryl-C1-4 alkyl containing one or more heteroatoms selected from the group consisting of N, O and S, where the C1-4 alkyl radical may be unsubstituted or mono or polysubstituted; or, if R, R1, R2, R3 may optionally be attached to the heteroarom. carbon atoms C1 to C9 of the acridine, are identical or different and independently of one another and are H, straight-chain or branched C1-8 alkyl, C3-7 cycloalkyl, straight-chain or branched C1-8 alkylcarbonyl, HO, straight-chain or branched C1-8 alkoxy, halogen, straight-chain or branched aryl-C1-8 alkoxy, trityloxy, trimethylsilyloxy, amino, mono(C1-4 alkyl)amino, di(C1-4 alkyl)amino, (C2-5 cycloalkyl)amino, morpholino, etc.; R5 = -SO2-X1 (where X1 = NMe2, hydroxy, alkoxy, etc.), C(O)-X2 (where X2 = (un)substituted alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, etc.), etc.] or physiol. acceptable salts thereof. These compds. are useful for treating benign and malignant tumors in humans and mammals. Thus, 6.66 g (11.06 mmol) polymer-bound N-benzyl-N-cyclohexylcarbodiimide (1.66 mmol/g) was added to a solution of 1.8 g (7.05 mmol) 1,3-dihydroxyacridine-9-carboxylic acid in 40 mL DMF. The mixture was heated at 60° and allowed to react for 30 min, treated with 1.03 g (5.64 mmol) 1-(6-methyl-2-pyridinyl)piperazine, and allowed to react for a further 4 h to give, after workup and silica gel chromatog., 2.3 g (1,3-dihydroxyacridin-9-yl)[4-(6-methylpyridin-2-yl)piperazin-1-yl]methanone (74.8%). The compds. I inhibited the proliferation of human tumor cell lines such as human cervical carcinoma cell line KB/Hela,

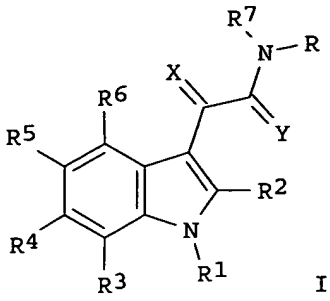
ovarian adenocarcinoma cell line SKOV3, human glioblastoma cell line SF-268, and lung carcinoma cell line NCI-H460 with EC50 of 0.007-0.293 μg/mL. Six compds. I were also tested for inhibiting the polymerization of tubulin and exhibited EC50 of 1.08-4.82.

L16 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1080885 HCAPLUS
DOCUMENT NUMBER: 142:56172
TITLE: Preparation of 1-(4-chlorobenzyl)indoles as tubulin polymerization inhibitors with apoptosis inducing activity
INVENTOR(S): Gerlach, Matthias; Schuster, Tilmann; **Emig, Peter**; Schmidt, Peter; Bassner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004108702 | A1 | 20041216 | WO 2004-EP5593 | 20040525 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1484329 | A1 | 20041208 | EP 2003-12868 | 20030606 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| EP 1595878 | A1 | 20051116 | EP 2004-11598 | 20040515 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| CA 2526663 | AA | 20041216 | CA 2004-2526663 | 20040525 |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 2003-476277P | P | 20030605 |
| EP 2003-12868 | A | 20030606 |
| EP 2004-11598 | A | 20040515 |
| WO 2004-EP5593 | W | 20040525 |

GI



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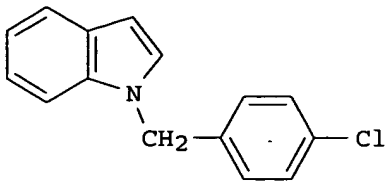
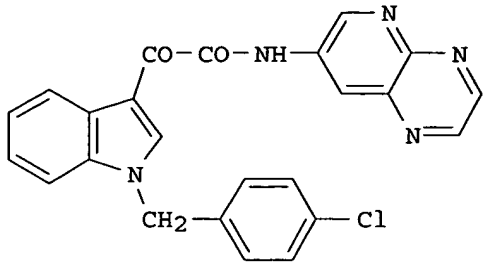


II



III

AB Title comounds I [R = (un)substituted heterocycle containing N, O, S heteroatoms; R1 = (un)substituted alkyl-aryl; R2 = H, (un)substituted alkyl; R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, etc.; R7 = alkylcarbonyl, alkoxycarbonyl; X, Y = S, O] and their pharmaceutically acceptable salts were prepared For example, oxalyl chloride acylation of chlorobenzylindole II, i.e., prepared from indole and 4-chlorobenzyl chloride, followed by pyrido[2,3-b]pyrazin-7-amine amidation afforded claimed chlorobenzylindole III in 68% yield. In human tubulin polymerization inhibition assays, 4-examples of compds. I exhibited EC50 values ranging from 0.71-1.26 μg/mL, i.e., the EC50 value of chlorobenzylindole III was 0.71 μg/mL. Compds. I are claimed to be useful as antitumor agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

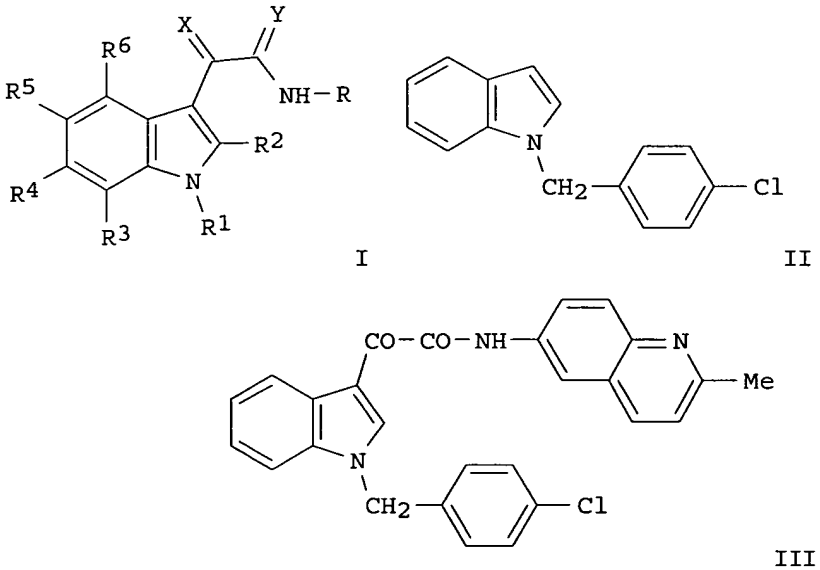
L16 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1054280 HCAPLUS
DOCUMENT NUMBER: 142:38145
TITLE: Preparation of 1-(4-chlorobenzyl)indoles as tubulin polymerization inhibitors with apoptosis inducing activity
INVENTOR(S): **Emig, Peter**; Gerlach, Matthias; Paulini, Klaus; Czech, Michael; Schuster, Tilmann; Schmidt, Peter; Baasner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

EP 1484329 A1 20041208 EP 2003-12868 20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
CA 2526663 AA 20041216 CA 2004-2526663 20040525
WO 2004108702 A1 20041216 WO 2004-EP5593 20040525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004266762 A1 20041230 US 2004-858751 20040602
PRIORITY APPLN. INFO.: US 2003-476277P P 20030605
EP 2003-12868 A 20030606
US 2003-476794P P 20030606
EP 2004-11598 A 20040515
US 2004-572025P P 20040517
WO 2004-EP5593 W 20040525

GI




I II III

AB Title comounds I [R = (un)substituted quinolyl, pyridopyrazinyl, indazolyl; R1 = alkyl-aryl; R2 = H; R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, etc.; X, Y = S, O] and their pharmaceutically acceptable salts were prepared For example, oxalyl chloride acylation of chlorobenzylindole II, i.e., prepared from indole and 4-chlorobenzyl chloride, followed by 6-amino-2-methylquinoline amidiation afforded claimed chlorobenzylindole III in 77% yield. In human tubulin polymerization inhibition assays, 6-examples of compds. I exhibited EC50 values ranging from 0.71-1.27 μg/mL, i.e., the EC50 value of chlorobenzylindole III

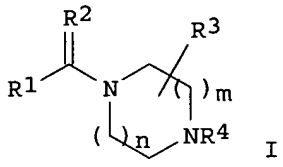
was 1.16 μg/mL. Compds. I are claimed to be useful as antitumor agents.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:20666 HCAPLUS
DOCUMENT NUMBER: 140:77166
TITLE: Preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating benign and malignant tumor diseases
INVENTOR(S): **Emig, Peter**; Gerlach, Matthias; Polymeropoulos, Emmanuel; Mueller, Gilbert; Schmidt, Peter; Baasner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris Gmbh, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2004002965 | A1 | 20040108 | WO 2003-EP6555 | | 20030620 |
| W: AU, BR, BY, CA, CN, CO, GE, HR, HU, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, UA, UZ, YU, ZA | | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | | | |
| AU 2003246571 | A1 | 20040119 | AU 2003-246571 | | 20030620 |
| EP 1517898 | A1 | 20050330 | EP 2003-761482 | | 20030620 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2003012294 | A | 20050412 | BR 2003-12294 | | 20030620 |
| CN 1665792 | A | 20050907 | CN 2003-815485 | | 20030620 |
| NZ 537916 | A | 20051125 | NZ 2003-537916 | | 20030620 |
| JP 2005538968 | T2 | 20051222 | JP 2004-516632 | | 20030620 |
| CA 2433983 | AA | 20031229 | CA 2003-2433983 | | 20030627 |
| US 2004097734 | A1 | 20040520 | US 2003-608520 | | 20030627 |
| ZA 2004009610 | A | 20050418 | ZA 2004-9610 | | 20041126 |
| NO 2005000428 | A | 20050125 | NO 2005-428 | | 20050125 |
| PRIORITY APPLN. INFO.: | | | US 2002-393027P | P | 20020629 |
| | | | WO 2003-EP6555 | W | 20030620 |

OTHER SOURCE(S): MARPAT 140:77166
GI



I

AB Title compds. [I; R1 = (substituted) fluoren-9-one, isoxazolyl, cinnolinyl, isothiazolyl, isoquinolinyl, 9H-fluorenyl, 9H-xanthenyl, 1H-pyrazolyl; R2 = O, S; R3 = H, (substituted) alkyl, halo, CO2H, CONH2;

R4 = (substituted) (hetero)aryl, alkylaryl, alkylhetaryl; m, n = 0-3], were prepared Thus, 9-fluorenone-4-carbonyl chloride in DMF was successively treated with N-methylmorpholine, 1-(3,5-dimethoxyphenyl)piperazine, and 1-benzotriazolyltripyrrolidinophosphonium hexafluorophosphate followed by stirring for 12 h at room temperature to give 79,3% 4-[4-(3,5-dimethoxyphenyl)piperazine-1-carbonyl]fluoren-9-one. The latter inhibited proliferation in XTT cytotoxicity test in human tumor cells with EC50 = 0,2-0,555 μg/mL.

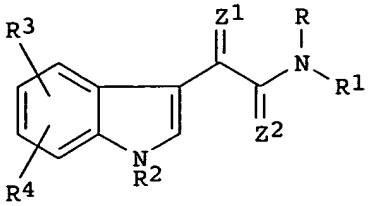
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:107333 HCAPLUS
DOCUMENT NUMBER: 136:167288
TITLE: Preparation of N-(6-quinolinyl)-3-indolylglyoxylamides as antitumor agents
INVENTOR(S): **Emig, Peter**; Bacher, Gerald; Reichert, Dietmar; Baasner, Silke; Aue, Beate; Nickel, Bernd; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002010152 | A2 | 20020207 | WO 2001-EP8644 | 20010726 |
| WO 2002010152 | A3 | 20020801 | | |
| W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| DE 10037310 | A1 | 20020207 | DE 2000-10037310 | 20000728 |
| US 2003100597 | A1 | 20030529 | US 2001-910140 | 20010720 |
| CA 2354210 | AA | 20020128 | CA 2001-2354210 | 20010726 |
| EP 1309585 | A2 | 20030514 | EP 2001-969522 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR | | | | |
| BR 2001012807 | A | 20030701 | BR 2001-12807 | 20010726 |
| JP 2004505075 | T2 | 20040219 | JP 2002-515883 | 20010726 |
| NZ 524404 | A | 20040827 | NZ 2001-524404 | 20010726 |
| RU 2270196 | C2 | 20060220 | RU 2003-105891 | 20010726 |
| ZA 2003000584 | A | 20030718 | ZA 2003-584 | 20030122 |
| NO 2003000382 | A | 20030220 | NO 2003-382 | 20030124 |
| BG 107560 | A | 20031031 | BG 2003-107560 | 20030214 |

PRIORITY APPLN. INFO.: DE 2000-10037310 A 20000728
WO 2001-EP8644 W 20010726

OTHER SOURCE(S): MARPAT 136:167288
GI



I

AB Title compds. [I; R = H, (substituted) alkyl, alkoxyalkyl, arylalkyloxycarbonyl, etc.; R1 = (substituted) (un)saturated and aromatic heterocyclyl especially (substituted) 2-, 3-, 4- and 8-quinolinyl and 2-, 3-, 4-quinolinylmethyl; R2 = H, (substituted) phenylalkyl, etc.; R3, R4 = H, OH, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, etc.; Z1 = O, S, H, OH; Z2 = O, S] and salts thereof were prepared Thus, (COCl)2 in ether was dropwise treated with 1-(4-chlorobenzyl)indole (preparation given) in ether under N2-atmosphere followed by reflux for 2 h and removal of solvent. The resulting reaction mixture in THF was dropwise treated with 6-amino-2-methylquinoline in THF followed by reflux for 4 h and then the reaction mixture was kept overnight at room temperature to give 77.3% N-(2-methyl-6-quinolinyl)-[1-(4-chlorobenzyl)indol-3-yl]glyoxylamide. The latter induced growth inhibition of e.g. human cervical carcinoma cell lines KB/HeLa with IC50 = 0.17 μM in a proliferation test.

L16 ANSWER 8 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:90014 HCAPLUS
DOCUMENT NUMBER: 136:134791
TITLE: Preparation of acridinylcarbonylpiperazines related compounds as anticancer drugs.
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Baasner, Silke; Bacher, Gerald; Beckers, Thomas; Aue, Beate
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002008194 | A1 | 20020131 | WO 2001-EP8263 | 20010718 |
| WO 2002008194 | C1 | 20030508 | | |
| W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| DE 10035927 | A1 | 20020307 | DE 2000-10035927 | 20000721 |
| EP 1301485 | A1 | 20030416 | EP 2001-969410 | 20010718 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR | | | | |
| BR 2001012591 | A | 20030722 | BR 2001-12591 | 20010718 |
| JP 2004504382 | T2 | 20040212 | JP 2002-514101 | 20010718 |
| NZ 524155 | A | 20050429 | NZ 2001-524155 | 20010718 |
| RU 2267488 | C2 | 20060110 | RU 2003-105283 | 20010718 |
| CA 2353360 | AA | 20020121 | CA 2001-2353360 | 20010720 |
| US 2002132821 | A1 | 20020919 | US 2001-910142 | 20010720 |

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|---|---|---|---|---|---|
| US 6706722 | B2 | 20040316 | | | |
| ZA 2002010411 | A | 20030226 | ZA 2002-10411 | | 20021223 |
| NO 2003000301 | A | 20030311 | NO 2003-301 | | 20030120 |
| BG 107507 | A | 20030930 | BG 2003-107507 | | 20030130 |
| PRIORITY APPLN. INFO.: | | | DE 2000-10035927 | A | 20000721 |
| | | | WO 2001-EP8263 | W | 20010718 |

OTHER SOURCE(S): MARPAT 136:134791
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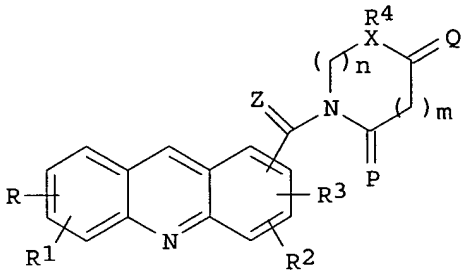

I

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, halo, aralkoxy, NO2, amino, alkoxycarbonylamino, cyano, cyanoalkyl, CO2H, alkoxycarbonyl, CF3, etc.; Z = O, S; P, Q = O, H2; X = N, CR5; R5 = H, alkyl; m, n = 0-3; R4 = (substituted) (unsatd.) alkyl, aryl, aralkyl, etc.], were prepared Thus, acridine-9-carboxylic acid in DMF was treated with N-methylmorpholine, Py-BOP, (1-benzotriazolyltripyrrolidinophosphoniu mhexafluorphosphate), and 1-(3,5-dimethoxyphenyl)piperazine in DMF. The mixture was stirred 12 h to give 84.2% 1-(3,5-dimethoxyphenyl)-4-(9-acridinylcarbonyl)piperazine. The latter inhibited KB/HeLa cell growth with IC50 <0.0003 μg/mL.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:90012 HCAPLUS
DOCUMENT NUMBER: 136:134790
TITLE: Preparation of quinolylcarbonylpiperazines and related compounds for treatment of tumors.
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Schmidt, Juergen; Nickel, Bernd; Kutscher, Bernhard
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002008192 | A1 | 20020131 | WO 2001-EP8261 | 20010718 |
| W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| DE 10035928 | A1 | 20020307 | DE 2000-10035928 | 20000721 |

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|---|---|---|---|---|---|
| EP 1305290 | A1 | 20030502 | EP 2001-957978 | | 20010718 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| BR 2001012589 | A | 20030520 | BR 2001-12589 | | 20010718 |
| JP 2004504381 | T2 | 20040212 | JP 2002-514099 | | 20010718 |
| NZ 524154 | A | 20050225 | NZ 2001-524154 | | 20010718 |
| RU 2265602 | C2 | 20051210 | RU 2003-105278 | | 20010718 |
| CA 2353369 | AA | 20020121 | CA 2001-2353369 | | 20010720 |
| US 2002103214 | A1 | 20020801 | US 2001-910141 | | 20010720 |
| US 6890926 | B2 | 20050510 | | | |
| ZA 2002010180 | A | 20030212 | ZA 2002-10180 | | 20021217 |
| NO 2003000298 | A | 20030120 | NO 2003-298 | | 20030120 |
| BG 107508 | A | 20030930 | BG 2003-107508 | | 20030130 |
| US 2004097530 | A1 | 20040520 | US 2003-713859 | | 20031114 |
| US 2004132747 | A1 | 20040708 | US 2003-741310 | | 20031219 |
| US 6936615 | B2 | 20050830 | | | |
| US 2005176744 | A1 | 20050811 | US 2005-105622 | | 20050414 |
| US 2005245523 | A1 | 20051103 | US 2005-152599 | | 20050614 |
| PRIORITY APPLN. INFO.: | | | DE 2000-10035928 | A | 20000721 |
| | | | WO 2001-EP8261 | W | 20010718 |
| | | | US 2001-910141 | A3 | 20010720 |
| | | | US 2003-741310 | A3 | 20031219 |

OTHER SOURCE(S): MARPAT 136:134790

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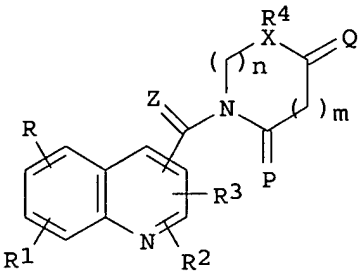

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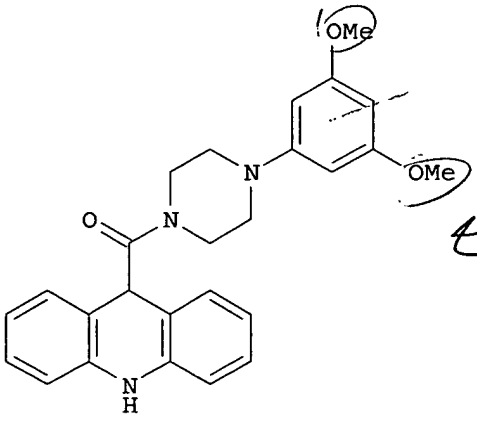


II

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, halo, aralkoxy, NO2, amino, cyano, CO2H, CF3, etc.; RR1, R2R3 = atoms to form condensed 6-membered aromatic rings; Z = O, S; X = N, CR5; R5 = H, alkyl; R4 = (substituted) (unsatd.) alkyl, aryl, aralkyl, etc.; P, Q = O, H2; m, n = 0-3], were prepared Thus, quinoline-4-carboxylic acid in DMF was treated with N-methylmorpholine, Py-BOP (1-benzotriazolyltripyrrolidinopho sphoniumhexafluorophosphate), and 1-(3,5-dimethoxyphenyl)piperazine in DMF. The mixture was stirred 12 h to give 78.3% 1-(3,5-dimethoxyphenyl)-4-(4-quinolylcarbonyl)piperazine. Title compound (II) (D-43411) showed antiproliferative activity with IC50 <0.0003 μg/mL against SKOV-3 tumor cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

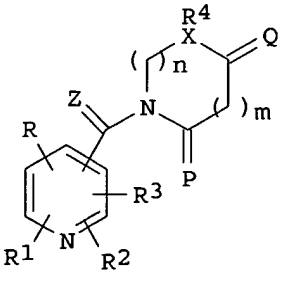
L16 ANSWER 10 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:90010 HCAPLUS
DOCUMENT NUMBER: 136:134789
TITLE: Preparation of pyridylcarbonylpiperazines and related compounds as anticancer drugs.
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Schmidt, Juergen; Kutscher, Bernhard; Nickel, Bernd; Storch, Anita
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002008190 | A2 | 20020131 | WO 2001-EP8262 | 20010718 |
| WO 2002008190 | A3 | 20020801 | | |
| W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| DE 10035908 | A1 | 20020307 | DE 2000-10035908 | 20000721 |
| EP 1305289 | A2 | 20030502 | EP 2001-960509 | 20010718 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR | | | | |
| BR 2001012711 | A | 20030520 | BR 2001-12711 | 20010718 |
| JP 2004516243 | T2 | 20040603 | JP 2002-514097 | 20010718 |
| NZ 524156 | A | 20051028 | NZ 2001-524156 | 20010718 |
| CA 2353353 | AA | 20020121 | CA 2001-2353353 | 20010720 |
| US 2002111354 | A1 | 20020815 | US 2001-910139 | 20010720 |
| US 6638935 | B2 | 20031028 | | |
| ZA 2003000545 | A | 20030212 | ZA 2003-545 | 20020121 |
| NO 2003000302 | A | 20030207 | NO 2003-302 | 20030120 |
| BG 107506 | A | 20030930 | BG 2003-107506 | 20030130 |

PRIORITY APPLN. INFO.: DE 2000-10035908 A 20000721
WO 2001-EP8262 W 20010718

OTHER SOURCE(S): MARPAT 136:134789
GI

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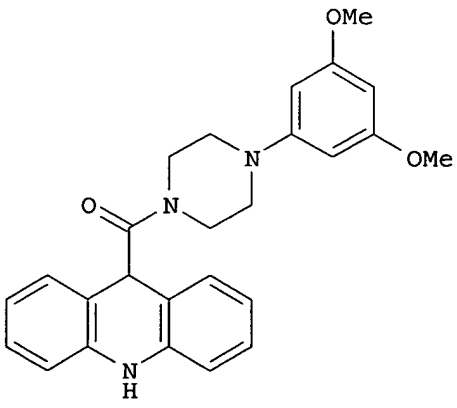


II

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, halo, aralkoxy, NO2, amino, cyano, CO2H, alkoxycarbonyl, CF3, etc.; RR1, R2R3 = atoms to form fused 6-membered aromatic rings; Z = O, S; P, Q = O, H2; X = N, CR5; m, n = 0-3; R4 = (substituted) (unsatd.) alkyl, aryl, aralkyl, etc.], were prepared Thus, pyridine-4-carboxylic acid in DMF was treated with N-methylmorpholine, Py-BOP (1-benzotriazolyltripyrrolidinophosphonium hexafluorphosphate), 1-(3,5-dimethoxyphenyl)piperazine followed by stirring for 24 h to give 82.3% 1-(3,5-dimethoxyphenyl)-4-(4-pyridylcarbonyl)piperazine. Title compound (II) inhibited L1210 tumor cells with IC50<0.0003 μg/mL.

L16 ANSWER 11 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:915607 HCAPLUS
DOCUMENT NUMBER: 136:193482
TITLE: New small-molecule tubulin inhibitors
AUTHOR(S): Bacher, G.; Beckers, T.; **Emig, P.**; Klenner, T.; Kutschert, B.; Nickel, B.
CORPORATE SOURCE: IUPAC Commission, Research & Development Oncology, ASTA Medica AG, Frankfurt, 60314, Germany
SOURCE: Pure and Applied Chemistry (2001), 73(9), 1459-1464
CODEN: PACHAS; ISSN: 0033-4545
PUBLISHER: International Union of Pure and Applied Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The variety of biol. agents directed toward the tubulin system exceeds those acting on DNA, making it an important target for cancer chemotherapy. However. the complicated chemical structures and restricted access to the natural resources, in combination with the development of drug resistance, limit the first generation of natural products. Considerable efforts in the search and synthesis of new synthetic compds., such as small mol. tubulin inhibitors, gave access to novel potential/promising drugs. Among these substances, two series of novel, easily accessible indole classes were identified as tubulin-destabilizing agents. Owing to the synthetic nature, potent in vitro and in vivo antitumoral activity, and efficacy against multidrug-resistant (MDR) tumors, D-24851 and D-64131 have significant potential in cancer treatment.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:858552 HCAPLUS
DOCUMENT NUMBER: 136:247463
TITLE: Synthesis and pharmacological evaluation of (indol-3-yl)alkylamides as potent analgesic agents
AUTHOR(S): Fouchard, Fabienne; Marchand, Pascal; Le Baut, Guillaume; **Emig, Peter**; Nickel, Bernd
CORPORATE SOURCE: Laboratoires de Chimie Organique et de Chimie Therapeutique, Faculte de Pharmacie, Nantes, 44035, Fr.
SOURCE: Arzneimittel-Forschung (2001), 51(10), 814-824
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:247463
AB A series of (indol-3-yl)alkylamides was synthesized and evaluated for analgesic activity. Two N-(pyridin-4-yl)acetamides, bearing benzyl or

4-fluorobenzyl moieties in 1-position of indole ring, exhibited promising analgesic properties (ED50 = 8.1 and 11 mg/kg p.o., resp.). The two test compds. were tested for their anti-inflammatory activity by carrageenin-induced edema in rat paw test. 4-Fluorobenzyl derivative whose ID50 was 0.085 ± 0.021 mmol/kg was selected as a lead compound for further pharmacomodulation.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:790429 HCAPLUS
DOCUMENT NUMBER: 136:200078
TITLE: Synthesis and characterization of the biologically active 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide
AUTHOR(S): Knaack, Martin; **Emig, Peter**; Bats, Jan W.; Kiesel, Michael; Muller, Arndt; Gunther, Eckhard
CORPORATE SOURCE: Infracor GmbH, Hanau, 63457, Germany
SOURCE: European Journal of Organic Chemistry (2001), (20), 3843-3847
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:200078
AB The spectroscopic characterization of the new potent tubulin inhibitor 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide (D-24851), which is under preclin. development, is described. The synthesis was optimized and follows a straightforward route from the unsubstituted indole via 1-(4-chlorobenzyl)indole and 1-[(4-chlorophenyl)methyl]-α-oxo-N-4-pyridinyl-1H-indole-3-acetyl chloride to the target compound, D-24851. The structure was assigned by sophisticated NMR expts., for example a 1,1-ADEQUATE experiment, and X-ray crystallog.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:467995 HCAPLUS
DOCUMENT NUMBER: 135:46111
TITLE: Preparation of N-(pyridin-4-yl) [1-(4-aminobenzyl)indol-3-yl]glyoxylamides as antitumor agents
INVENTOR(S): Guenther, Eckhard; **Emig, Peter**; Reichert, Dietmar; Le Baut, Guillaume; Nickel, Bernd; Bacher, Gerald
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 19962300 | A1 | 20010628 | DE 1999-19962300 | 19991223 |
| US 2001014690 | A1 | 20010816 | US 2000-736431 | 20001215 |
| US 6432987 | B2 | 20020813 | | |
| CA 2395259 | AA | 20010705 | CA 2000-2395259 | 20001219 |

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|---|---|---|---|---|---|
| WO 2001047913 | A2 | 20010705 | WO 2000-EP12947 | | 20001219 |
| W: AT, AU, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | | |
| BR 2000016712 | A | 20020903 | BR 2000-16712 | | 20001219 |
| EP 1240157 | A2 | 20020918 | EP 2000-983349 | | 20001219 |
| EP 1240157 | B1 | 20040211 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR | | | | | |
| JP 2003519137 | T2 | 20030617 | JP 2001-549383 | | 20001219 |
| AT 259364 | E | 20040215 | AT 2000-983349 | | 20001219 |
| AU 772745 | B2 | 20040506 | AU 2001-20119 | | 20001219 |
| PT 1240157 | T | 20040630 | PT 2000-983349 | | 20001219 |
| NZ 519977 | A | 20040827 | NZ 2000-519977 | | 20001219 |
| ES 2215768 | T3 | 20041016 | ES 2000-983349 | | 20001219 |
| NZ 533731 | A | 20050324 | NZ 2000-533731 | | 20001219 |
| RU 2266280 | C2 | 20051220 | RU 2002-120462 | | 20001219 |
| ZA 2002004896 | A | 20021220 | ZA 2002-4896 | | 20020619 |
| NO 2002003039 | A | 20020809 | NO 2002-3039 | | 20020621 |
| BG 106924 | A | 20030430 | BG 2002-106924 | | 20020716 |
| PRIORITY APPLN. INFO.: | | | DE 1999-19962300 | A | 19991223 |
| | | | WO 2000-EP12947 | W | 20001219 |

OTHER SOURCE(S): MARPAT 135:46111

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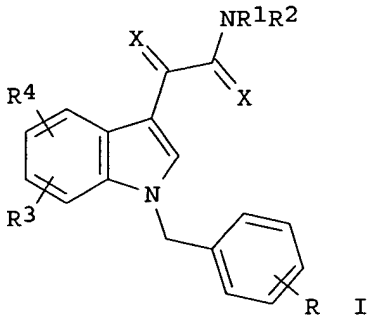


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AB Title compds. [I; R1 = H, (substituted) alkyl, benzyloxycarbonyl, t-butoxycarbonyl, OAc; R2 = (substituted) Ph, pyridinyl, pyrimidinyl, etc.; or R1R2 = (substituted) (homo)piperazinyl; R3, R4 = H, alkyl, cycloalkyl, alkanoyl, alkoxy, halo, PhCH2O, NO2, amino, etc.; R = NO2, amino, (di)alkylamino, cycloalkylamino, phenylalkylamino, (hetero)aroylamino, etc.; X = O, S] were prepared as antitumor agents (no data). Thus, (COCl)2 in Et2O at 0° was treated dropwise with indole in Et2O and refluxed for 3 h followed by dropwise addition of 4-aminopyridine in THF at 5° and reflux over night to give 43.3% N-(pyridin-4-yl) (indol-3-yl)glyoxylamide. The product was treated with 4-nitrobenzyl chloride to give 64% N-(pyridin-4-yl) [1-(4-nitrobenzyl)indol-3-yl]glyoxylamide (D-68836). The latter was subjected to catalytic hydrogenation to give 94% N-(pyridin-4-yl) [1-(4-aminobenzyl)indol-3-yl]glyoxylamide (D-68838). D-68838 was said to inhibit polymerization of tubulin.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:247170 HCAPLUS
DOCUMENT NUMBER: 134:261240
TITLE: Indolyl-3-glyoxylic acid derivatives comprising therapeutically valuable properties
INVENTOR(S): Nickel, Bernd; Klenner, Thomas; Bacher, Gerald; Beckers, Thomas; **Emig, Peter**; Engel, Juergen; Bruyneel, Erik; Kamp, Guenter; Peters, Kirsten
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001022954 | A2 | 20010405 | WO 2000-EP9390 | 20000926 |
| WO 2001022954 | A3 | 20020328 | | |
| W: AU, BG, BR, BY, CA, CN, CZ, DZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19946301 | A1 | 20010419 | DE 1999-19946301 | 19990928 |
| US 2003114511 | A1 | 20030619 | US 2000-492531 | 20000127 |
| US 6693119 | B2 | 20040217 | | |
| CA 2386069 | AA | 20010405 | CA 2000-2386069 | 20000926 |
| EP 1218006 | A2 | 20020703 | EP 2000-967789 | 20000926 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003510274 | T2 | 20030318 | JP 2001-526166 | 20000926 |
| EE 200200169 | A | 20030415 | EE 2002-169 | 20000926 |
| BR 2000014378 | A | 20030729 | BR 2000-14378 | 20000926 |
| NZ 517988 | A | 20041029 | NZ 2000-517988 | 20000926 |
| AU 783436 | B2 | 20051027 | AU 2000-77829 | 20000926 |
| NO 2002001367 | A | 20020522 | NO 2002-1367 | 20020319 |
| ZA 2002002556 | A | 20030704 | ZA 2002-2556 | 20020402 |
| BG 106639 | A | 20021229 | BG 2002-106639 | 20020423 |
| US 2004171668 | A1 | 20040902 | US 2003-686809 | 20031017 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| DE 1999-19946301 | A | 19990928 |
| DE 1998-19814838 | A | 19980402 |
| US 1999-285058 | A2 | 19990402 |
| US 2000-492531 | A1 | 20000127 |
| WO 2000-EP9390 | W | 20000926 |

OTHER SOURCE(S): MARPAT 134:261240
AB The invention relates to the use of N-substituted indol-3- glyoxylamides of for treating tumors, in particular, in cases of drug resistance and metastatic carcinoma, and as angiogenesis inhibitors having distinctly fewer side effects, in particular, distinctly lower neurotoxicity. The invention also relates to medicaments containing the inventive compds.

L16 ANSWER 16 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:58000 HCAPLUS
DOCUMENT NUMBER: 134:290069
TITLE: D-24851, a novel synthetic microtubule inhibitor, exerts curative antitumoral activity in vivo, shows

efficacy toward multidrug-resistant tumor cells, and lacks neurotoxicity

AUTHOR(S): Bacher, Gerald; Nickel, Bernd; **Emig, Peter**; Vanhoefer, Udo; Seeber, Siegfried; Shandra, Alexei; Klenner, Thomas; Beckers, Thomas

CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt am Main, 60314, Germany

SOURCE: Cancer Research (2001), 61(1), 392-399
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N-(pyridin-4-yl)-[1-(4-chlorbenzyl)indol-3-yl]glyoxylamide (D-24851) is a novel synthetic compound that was identified in a cell-based screening assay to discover cytotoxic drugs. D-24851 destabilizes microtubules and blocks cell cycle transition specifically at G2-M phase. The binding site of D-24851 does not overlap with the tubulin binding sites of known microtubule-destabilizing agents like vincristine or colchicine. In vitro, D-24851 has potent cytotoxic activity toward a panel of established human tumor cell lines including SKOV3 ovarian cancer, U87 glioblastoma, and ASPC-1 pancreatic cancer cells. In vivo, oral D-24851 treatment induced complete tumor regressions (cures) in rats bearing Yoshida AH13 sarcomas. Of importance is that the administration of curative doses of D-24851 to the animals revealed no systemic toxicity in terms of body weight loss and neurotoxicity in contrast to the administration of paclitaxel or vincristine. Interestingly, multidrug-resistant cell lines generated by vincristine-driven selection or transfection with the Mr 170,000 P-glycoprotein encoding cDNA were rendered resistant toward paclitaxel, vincristine, or doxorubicin but not towards D-24851 when compared with the parental cells. Because of its synthetic nature, its oral applicability, its potent in vitro and in vivo antitumoral activity, its efficacy against multidrug-resistant tumors, and the lack of neurotoxicity, D-24851 may have significant potential for the treatment of various malignancies.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:659229 HCAPLUS

DOCUMENT NUMBER: 131:271807

TITLE: Preparation of indolylglyoxylamides as antitumor agents

INVENTOR(S): Nickel, Bernd; Szelenyi, Istvan; Schmidt, Jurgen; **Emig, Peter**; Reichert, Dietmar; Gunther, Eckhard; Brune, Kay

PATENT ASSIGNEE(S): Asta Medica A.-G., Germany

SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9951224 | A1 | 19991014 | WO 1999-EP1918 | 19990322 |
| W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |

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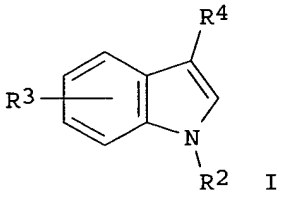
|---|---|---|---|---|
| DE 19814838 | A1 | 19991014 | DE 1998-19814838 | 19980402 |
| DE 19814838 | C2 | 20010118 | | |
| CA 2326833 | AA | 19991014 | CA 1999-2326833 | 19990322 |
| AU 9929349 | A1 | 19991025 | AU 1999-29349 | 19990322 |
| AU 768510 | B2 | 20031218 | | |
| BR 9909902 | A | 20001226 | BR 1999-9902 | 19990322 |
| EP 1071420 | A1 | 20010131 | EP 1999-910372 | 19990322 |
| EP 1071420 | B1 | 20050914 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200002853 | T2 | 20010221 | TR 2000-200002853 | 19990322 |
| EE 200000581 | A | 20020215 | EE 2000-581 | 19990322 |
| EE 4354 | B1 | 20041015 | | |
| JP 2002510622 | T2 | 20020409 | JP 2000-541995 | 19990322 |
| NZ 507084 | A | 20031031 | NZ 1999-507084 | 19990322 |
| AT 304352 | E | 20050915 | AT 1999-910372 | 19990322 |
| RU 2262339 | C2 | 20051020 | RU 2000-128035 | 19990322 |
| US 6232327 | B1 | 20010515 | US 1999-285058 | 19990402 |
| US 2003114511 | A1 | 20030619 | US 2000-492531 | 20000127 |
| US 6693119 | B2 | 20040217 | | |
| NO 2000004916 | A | 20001201 | NO 2000-4916 | 20000929 |
| HR 2000000643 | A1 | 20010430 | HR 2000-643 | 20001002 |
| BG 104849 | A | 20010531 | BG 2000-104849 | 20001012 |
| ZA 2000006150 | A | 20010111 | ZA 2000-6150 | 20001031 |
| US 2003023093 | A1 | 20030130 | US 2001-810604 | 20010319 |
| HK 1036408 | A1 | 20050218 | HK 2001-107405 | 20011024 |
| US 2003195360 | A1 | 20031016 | US 2002-309204 | 20021204 |
| US 2004171668 | A1 | 20040902 | US 2003-686809 | 20031017 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| DE 1998-19814838 | A | 19980402 |
| WO 1999-EP1918 | W | 19990322 |
| US 1999-285058 | A1 | 19990402 |
| DE 1999-19946301 | A | 19990928 |
| US 2000-492531 | A1 | 20000127 |
| US 2001-810604 | A1 | 20010319 |

OTHER SOURCE(S): MARPAT 131:271807

GI




I

AB Title compds. [I; R2 = H or (un)substituted alkyl; R3 = H or 1 or 2 of halo, alkyl, alkoxy, etc.; R4 = C(:X)C(:X)NRR1; R = H, (un)substituted alkyl, CO2CH2Ph, etc.; R1 = (un)substituted Ph, -pyridyl, -pyrimidyl, etc.; RR1 = (CH2CH2)2NR7; R7 = alkyl, Ph, CHPh2, etc.; X = O or S] were prepared Thus, indole was N-alkylated by 4-FC6H4CH2Cl and the product acylated by (COCl)2 to give, after 4-aminopyridine amidation, I (R2 = CH2C6H4F-4, R3 = H, R4 = COCONHR1, R1 = 4-pyridyl). Data for biol. activity of I were given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:65867 HCAPLUS
DOCUMENT NUMBER: 130:223153
TITLE: New N-(Pyridin-4-yl)-(indol-3-yl)acetamides and Propanamides as Antiallergic Agents
AUTHOR(S): Menciu, Cecilia; Duflos, Muriel; Fouchard, Fabienne; Le Baut, Guillaume; **Emig, Peter**; Achterrath, Ute; Szelenyi, Istvan; Nickel, Bernd; Schmidt, Juergen; Kutscher, Bernhard; Guenther, Eckhardt
CORPORATE SOURCE: Department of Organic Chemistry and Medicinal Chemistry, Faculty of Pharmacy, Nantes, 44035, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(4), 638-648
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of new N-(pyridin-4-yl)-(indol-3-yl)alkylamides has been prepared in the search of novel antiallergic compds. Synthesis of the desired Et (2-methyindol-3-yl)acetates was achieved by indolization under Fischer conditions; Japp-Klingemann method followed by 2-decarboxylation afforded the Et (indol-3-yl)alkanoates. Amidification was successfully carried out by condensation of the acids or their N-aryl(methyl) derivs. with 4-aminopyridine promoted by 2-chloro-1-methylpyridinium iodide. Efforts to improve the antiallergic potency of the title series by variation of the indole substituents (R1, R2, R) and the length of the alkanoic chain (n = 1, 2, 3) led to the selection of N-(pyridin-4-yl)-[1-(4-fluorobenzyl)indol-3-yl]acetamide (I), out of 41 compds. This amide was 406-fold more potent than astemizole in the ovalbumin-induced histamine release assay, using guinea pig peritoneal mast cells, with an IC50 = 0.016 μM. Its inhibitory activity in IL-4 production test from Th-2 cells was identical to that of the reference histamine antagonist (IC50 = 8.0 μM) and twice higher in IL-5 assay: IC50 = 1.5 and 3.3 μM, resp. In vivo antiallergic activity evaluation confirmed efficiency of I in sensitized guinea pig late phase eosinophilia inhibition, after parenteral and oral administration at 5 and 30 mg/kg, resp. Its efficiency in inhibition of microvascular permeability was assessed in two rhinitis models; ovalbumin and capsaicin-induced rhinorrhea could be prevented after topical application of submicromolar concns. of 45 (IC50 = 0.25 and 0.30 μM); and it also exerted significant inhibitory effect in the first test after i.v. and oral administration, with ID50 = 0.005 and 0.46 mg/kg.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:46386 HCAPLUS
DOCUMENT NUMBER: 130:100782
TITLE: Polymorphism and desolvation of flupirtine maleate
AUTHOR(S): Landgraf, Karl-Friedrich; Olbrich, Alfred; Pauluhn, Siegfried; **Emig, Peter**; Kutscher, Bernhard; Stange, Hans
CORPORATE SOURCE: ASTA Medica A.-G., Dresden, Germany
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (1998), 46(3), 329-337
CODEN: EJPBEL; ISSN: 0939-6411
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Crystallizates of the analgesic agent flupirtine maleate (Katadolon; ASTA Medica, Dresden, Germany) obtained from isopropanol are examined by x-ray diffractometry, polarization microscopy and thermoanal. Depending on the crystallizing conditions, the modifications A and B as well as an isopropanol

solvate are observed The inversion temperature A → B of the enantiotropic modifications is 164° (differential scanning calorimetry (DSC) onset). During thermal desolvation, modification B is formed well below the inversion temperature In concentrated isopropanol suspensions, the solvate and modification B are rapidly transformed into modification A. It is shown how phase-pure products consisting of modification A, which is better wettable with water and stable at room temperature, can be obtained.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:709053 HCAPLUS
DOCUMENT NUMBER: 129:316153
TITLE: Preparation of pure flupirtin maleate and its A crystal modification.
INVENTOR(S): Olbrich, Alfred; **Emig, Peter**; Kutscher, Bernhard; Landgraf, Karl-Friedrich; Pauluhn, Siegfried; Stange, Hans
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9847872 | A1 | 19981029 | WO 1998-EP2118 | 19980411 |
| W: AU, BR, CA, CN, CZ, HU, IS, JP, NO, PL, RU, SK | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19716984 | A1 | 19981029 | DE 1997-19716984 | 19970423 |
| AU 9873346 | A1 | 19981113 | AU 1998-73346 | 19980411 |
| EP 977736 | A1 | 20000209 | EP 1998-920511 | 19980411 |
| EP 977736 | B1 | 20030924 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001523236 | T2 | 20011120 | JP 1998-544940 | 19980411 |
| AT 250579 | E | 20031015 | AT 1998-920511 | 19980411 |
| PT 977736 | T | 20040227 | PT 1998-920511 | 19980411 |
| ES 2207832 | T3 | 20040601 | ES 1998-920511 | 19980411 |
| ZA 9803376 | A | 19980703 | ZA 1998-3376 | 19980422 |
| US 5959115 | A | 19990928 | US 1998-64790 | 19980423 |

PRIORITY APPLN. INFO.: DE 1997-19716984 A 19970423
WO 1998-EP2118 W 19980411

AB Flupirtin maleate (I) was prepared by hydrogenation of 2-amino-3-nitro-6-(4-fluorobenzylamino)pyridine (II) using Raney Ni, acylation with EtO2CCl, and treatment of the resulting flupirtin with maleic acid. Thus, II in Me2CHOH was hydrogenated over Raney Ni at 65° and 5 bar H2; EtO2CCl and Et3N were added followed by stirring at 60°, filtration at 50-60° into a solution of maleic acid in H2O to precipitate I (89.6% yield). I A crystal modification was obtained by stirring I A and B crystal modification mixture in Me2CHOH.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:175908 HCAPLUS

DOCUMENT NUMBER: 128:217285
TITLE: Preparation of new, N-substituted indole-3-glyoxylamides as antiasthmatics, antiallergic agents and immunosuppressants/immunomodulators
INVENTOR(S): Lebaut, Guillaume; Menciu, Cecilia; Kutscher, Bernhard; **Emig, Peter**; Szelenyi, Stefan; Brune, Kay
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9809946 | A1 | 19980312 | WO 1997-EP4474 | 19970816 |
| W: AU, BR, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SG, SK, TR, UA | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19636150 | A1 | 19980312 | DE 1996-19636150 | 19960906 |
| AU 9740158 | A1 | 19980326 | AU 1997-40158 | 19970816 |
| AU 726521 | B2 | 20001109 | | |
| EP 931063 | A1 | 19990728 | EP 1997-937586 | 19970816 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1227542 | A | 19990901 | CN 1997-197128 | 19970816 |
| BR 9712808 | A | 19991123 | BR 1997-12808 | 19970816 |
| JP 2000505098 | T2 | 20000425 | JP 1998-512167 | 19970816 |
| JP 3296437 | B2 | 20020702 | | |
| NZ 334476 | A | 20000526 | NZ 1997-334476 | 19970816 |
| IL 127798 | A1 | 20030731 | IL 1997-127798 | 19970816 |
| CN 1496980 | A | 20040519 | CN 2002-2002132061 | 19970816 |
| RU 2237661 | C2 | 20041010 | RU 1999-106782 | 19970816 |
| ZA 9707475 | A | 19980219 | ZA 1997-7475 | 19970820 |
| CA 2215013 | AA | 19980306 | CA 1997-2215013 | 19970904 |
| CA 2215013 | C | 20020305 | | |
| US 6008231 | A | 19991228 | US 1997-925326 | 19970908 |
| TW 550256 | B | 20030901 | TW 1997-86112985 | 19970930 |
| NO 9901071 | A | 19990304 | NO 1999-1071 | 19990304 |
| NO 314725 | B1 | 20030512 | | |
| US 6344467 | B1 | 20020205 | US 1999-409263 | 19990930 |
| US 2002161025 | A1 | 20021031 | US 2002-58836 | 20020130 |
| NO 2003000481 | A | 19990304 | NO 2003-481 | 20030130 |
| US 2003207892 | A1 | 20031106 | US 2003-402931 | 20030401 |
| US 6919344 | B2 | 20050719 | | |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| DE 1996-19636150 | A | 19960906 |
| WO 1997-EP4474 | W | 19970816 |
| US 1997-925326 | A3 | 19970908 |
| US 1999-409263 | A3 | 19990930 |
| US 2002-58836 | B1 | 20020130 |

OTHER SOURCE(S): MARPAT 128:217285
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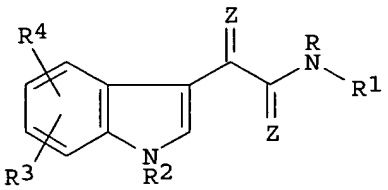

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AB The title compds. [I; R = H, (un)substituted C1-6 alkyl; R1 = (un)substituted Ph, pyridyl, pyrimidinyl, etc.; RR1 = atoms to close (N-substituted) piperazine ring; R2 = H, (un)substituted C1-6 alkyl, (un)substituted benzoyl; R3, R4 = H, OH, C1-6 alkyl, C3-7 cycloalkyl, halo, NO2, amino, benzyloxy, etc.; Z = O, S] and their acid salts were prepared, e.g., by N-alkylation of indoles with R2-bearing reactants followed by acylation with a dicarbonyl halide and amidation of the remaining acid halide function. For example, a title compound I (R = R3 = R4 = H, R1 = 4-pyridyl, R2 = 4-FC6H4CH2, Z = O) (preparation by benzylation of indole with 4-FC6H4CH2Cl, acylation of the intermediate with (COCl)2 and amidation of the acyl chloride with 4-aminopyridine given) at 10 mg/kg i.p. in guinea pigs gave 55.4% inhibition of allergen-induced late-phase eosinophilia, vs. 47.0 for cyclosporin A.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:534403 HCAPLUS
DOCUMENT NUMBER: 125:221765
TITLE: Ring-rearrangement during the Mitsunobu alkylation of phthalazinones and indazolols
AUTHOR(S): Knaack, Martina; Fleischhauer, Ilona; Charpentier, Patricia; **Emig, Peter**; Kutscher, Bernhard; Mueller, Arndt
CORPORATE SOURCE: Degussa A.-G., Hanau, D-63403, Germany
SOURCE: Liebigs Annalen (1996), (9), 1477-1482
CODEN: LANAEM; ISSN: 0947-3440
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The Mitsunobu alkylation of substituted phthalazinones and indazolols with cyclic hydroxy- and hydroxymethyl-substituted amines was investigated. In addition to the expected derivs. ring-narrowed and ring-enlarged rearrangement products were isolated and characterized by NMR. The occurrence of these products is explained by the existence of a bicyclic intermediate. The results of the reaction of phthalazinones with optically active amine compds. show a stereospecific reaction mechanism. The reaction of the phthalazinones leads to N-substituted products, while in the case of the indazolols O-substituted derivs. were isolated. A postulated bicyclic intermediate, 1-methyl-1-azoniabicyclo[3.2.0]heptane, was synthesized as chloride.

L16 ANSWER 23 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:273624 HCAPLUS
DOCUMENT NUMBER: 124:316986
TITLE: Preparation of N-benzylindoles and -benzopyrazoles with antiasthmatic, antiallergic, antiinflammatory, and immunomodulating activity.
INVENTOR(S): Le Baut, Guillaume; Fouchard, Fabienne; Kutscher,

Bernhard; **Emig, Peter**; Schmidt, Juergen; Szelenyi, Stefan; Fleischhauer, Ilona
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 19511916 | A1 | 19960208 | DE 1995-19511916 | 19950331 |
| CA 2195850 | AA | 19960215 | CA 1995-2195850 | 19950720 |
| WO 9604266 | A2 | 19960215 | WO 1995-EP2867 | 19950720 |
| WO 9604266 | A3 | 19960517 | | |
| W: AU, BR, BY, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SI, SK, UA, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9531626 | A1 | 19960304 | AU 1995-31626 | 19950720 |
| EP 775131 | A2 | 19970528 | EP 1995-927679 | 19950720 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 10503501 | T2 | 19980331 | JP 1995-506137 | 19950720 |
| TW 434227 | B | 20010516 | TW 1995-84107752 | 19950726 |
| ZA 9506382 | A | 19960313 | ZA 1995-6382 | 19950731 |
| IL 114795 | A1 | 19991130 | IL 1995-114795 | 19950801 |
| EG 21559 | A | 20011231 | EG 1995-644 | 19950801 |
| NO 9700412 | A | 19970227 | NO 1997-412 | 19970130 |
| FI 9701334 | A | 19970401 | FI 1997-1334 | 19970401 |
| US 5965582 | A | 19991012 | US 1997-776616 | 19970512 |

PRIORITY APPLN. INFO.: DE 1994-4427393 A1 19940803
DE 1995-19511916 A 19950331
WO 1995-EP2867 W 19950720

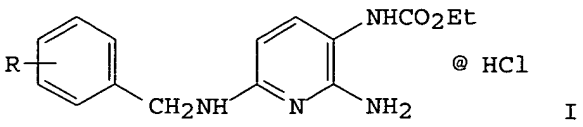
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I, II; R1, R10, R11, R12 = alkyl, cycloalkyl, alkoxy, (substituted) aryl, aroyl, quinolylmethyl, etc.; R2, R3 = H, alkyl, cycloalkyl, NO2, amino; R4 = H, alkyl, cycloalkyl; R5 = N-alkyl-2-pyrrolidinyl, amino; W = CH, NH; Y = O, S; X = CH, N, bond], were prepared Thus, title compound (III), prepared from indole-3-acetic acid by benzylation with 4-fluorobenzyl chloride, partial hydrolysis with NaOH in H2O/EtOH, and amidation with 4-aminopyridine/DCC, inhibited allergen-induced histamine release in rat mast cells with IC50 = 0.016 μmol/L.

L16 ANSWER 24 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:605183 HCAPLUS
DOCUMENT NUMBER: 121:205183
TITLE: Synthesis and Quantitative Structure-Activity Relationships of Anticonvulsant 2,3,6-Triaminopyridines
AUTHOR(S): Seydel, Joachim K.; Schaper, Klaus-J.; Coats, Eugene A.; Cordes, Hans P.; **Emig, Peter**; Engel, Juergen; Kutscher, Bernhard; Polymeropoulos, Emmanuel

E.
CORPORATE SOURCE: Borstel Research Institute, Borstel, 23845, Germany
SOURCE: Journal of Medicinal Chemistry (1994), 37(19), 3016-22
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI




I

AB The synthesis of 2,3,6-triaminopyridine derivs., , e.g. I (R = H, 3-F, 4-Cl, 4-Ac, 4-NHAc, 2-Me, 2-OH, 4-CF3, 2,4-F2, 2,4-Me2, 2,6-Me2 2,4,6-Me3), representing a unique chemical structure for anticonvulsants, is described. The synthetic program was performed (a) to identify more potent analogs, (b) to determine structural properties controlling potency as well as neurotoxicity, and (c) to reduce the requirements for animal testing. As a result, besides other structural properties, the overall mol. lipophilicity (log k', octanol-coated column) explained changes in anticonvulsant potency and neurotoxicity. Mimicking the interaction of the amphiphilic triaminopyridines with biol. membranes, NMR expts. in the presence of lecithin vesicles were conducted in order to measure the phospholipid-binding parameter log Δ(1/T2). Replacement of log k' with log Δ(1/T2) in the correlation anal. afforded a more significant equation describing the anticonvulsant activity of 21 derivs.

L16 ANSWER 25 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:569743 HCAPLUS
DOCUMENT NUMBER: 121:169743
TITLE: QSAR analysis of time- and dose-dependent in vivo drug effects using artificial neural networks
AUTHOR(S): Schapper, Klaus-Juergen; Wiese, Michael; Dieter, Reinhold; **Emig, Peter**; Engel, Juergen; Kutscher, Bernhard; Polymeropoulos, Emmanuel E.
CORPORATE SOURCE: Borstel Res. Inst., Borstel, D-2061, Germany
SOURCE: Trends QSAR Mol. Modell. 92, Proc. Eur. Symp. Struct.-Act. Relat.: QSAR Mol. Modell., 9th (1993), Meeting Date 1992, 546-9. Editor(s): Wermuth, Camille-Georges. ESCOM: Leiden, Neth.
CODEN: 59XTAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB QSAR anal. of time- and dose-dependent in vivo anticonvulsant activities of triaminobenzenes was carried out. Property-dependent activities were estimated Complete dos-response curves were obtained.

L16 ANSWER 26 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:426878 HCAPLUS
DOCUMENT NUMBER: 121:26878
TITLE: Pharmaceutical composition consisting of flupirtine and morphine for the treatment of pain and to avoid a morphine addiction
INVENTOR(S): Nickel, Bernd; Lobisch, Michael; Szelenyi, Stefan; Engel, Juergen; **Emig, Peter**; Pergande, Gabriela

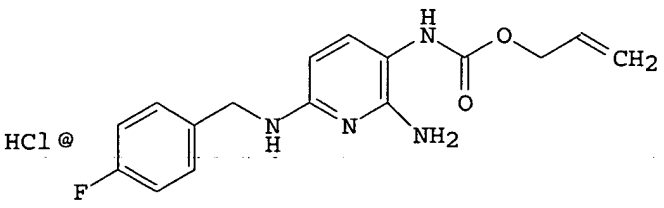
PATENT ASSIGNEE(S): ASTA Medica AG, Germany
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 595311 | A1 | 19940504 | EP 1993-117472 | 19931028 |
| EP 595311 | B1 | 19970122 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| DE 4236752 | A1 | 19940505 | DE 1992-4236752 | 19921030 |
| US 5521178 | A | 19960528 | US 1993-141678 | 19931027 |
| AT 147979 | E | 19970215 | AT 1993-117472 | 19931028 |
| ES 2099344 | T3 | 19970516 | ES 1993-117472 | 19931028 |
| CA 2102072 | AA | 19940501 | CA 1993-2102072 | 19931029 |
| CA 2102072 | C | 20050104 | | |
| BR 9304431 | A | 19940607 | BR 1993-4431 | 19931029 |
| JP 06211663 | A2 | 19940802 | JP 1993-271730 | 19931029 |
| JP 3665354 | B2 | 20050629 | | |
| HU 66085 | A2 | 19940928 | HU 1993-3089 | 19931029 |
| HU 219907 | B | 20010928 | | |

PRIORITY APPLN. INFO.: DE 1992-4236752 A 19921030

AB Coadministration of flupirtine and morphine results in additive analgesic activity, reduced dependence on morphine, and no development of tolerance to flupirtine. Thus, the excitation, rearing behavior, and rigidity seen in rats after withdrawal from morphine in long-term expts. were markedly less in rats which had been injected with morphine and flupirtine. A preferred dosage form was a tablet containing 50-500 mg flupirtine and 10-250 mg morphine as salts.

L16 ANSWER 27 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:560063 HCAPLUS
DOCUMENT NUMBER: 119:160063
TITLE: New triaminopyridines with a central analgesic activity
AUTHOR(S): **Emig, P.**; Nickel, B.; Weischer, C.-H.; Szelenyi, I.; Engel, J.
CORPORATE SOURCE: Forschung Asta Med. AG, Frankfurt/Main, Germany
SOURCE: Arzneimittel-Forschung (1993), 43(6), 627-31
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
GI




I

AB 2-Amino-3-[[[(3-propenyl)oxy]carbonyl]amino]-6-[(4-fluorobenzyl)amino]pyridine hydrochloride [D-19050; 2-propenyl [2-amino-6-[[(4-fluorophenyl)methyl]amino]-3-pyridinyl]carbamate] (I) is a centrally and peripherally acting analgesic with rapid onset, long duration of action and a good therapeutic range. D-19050 can be obtained in a 5-step-preparation starting from 2,6-dichloropyridine. I is a flupirtine analog.

L16 ANSWER 28 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:120908 HCAPLUS
DOCUMENT NUMBER: 116:120908
TITLE: Flupirtine as spasmolytic
INVENTOR(S): Lobisch, Michael; Venhaus, Ralph; Nickel, Bernd; Szelenyi, Istvan; Engel, Juergen; **Emig, Peter**
PATENT ASSIGNEE(S): Asta Pharma A.-G., Germany
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4122166 | A1 | 19920116 | DE 1991-4122166 | 19910704 |
| IN 172468 | A | 19930814 | IN 1991-CA421 | 19910604 |
| EP 467164 | A2 | 19920122 | EP 1991-111124 | 19910704 |
| EP 467164 | A3 | 19920415 | | |
| EP 467164 | B1 | 19960131 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| EP 659410 | A2 | 19950628 | EP 1995-101189 | 19910704 |
| EP 659410 | A3 | 19951025 | | |
| EP 659410 | B1 | 20011017 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| AT 133564 | E | 19960215 | AT 1991-111124 | 19910704 |
| ES 2082887 | T3 | 19960401 | ES 1991-111124 | 19910704 |
| AT 206919 | E | 20011115 | AT 1995-101189 | 19910704 |
| ES 2164111 | T3 | 20020216 | ES 1995-101189 | 19910704 |
| CZ 280879 | B6 | 19960417 | CZ 1991-2101 | 19910708 |
| SK 279567 | B6 | 19990111 | SK 1991-2101 | 19910708 |
| RO 108220 | B1 | 19940331 | RO 1991-147972 | 19910709 |
| US 5162346 | A | 19921110 | US 1991-726408 | 19910710 |
| CA 2046943 | AA | 19920115 | CA 1991-2046943 | 19910712 |
| CA 2046943 | C | 19960312 | | |
| NO 9102758 | A | 19920115 | NO 1991-2758 | 19910712 |
| AU 9180403 | A1 | 19920116 | AU 1991-80403 | 19910712 |
| AU 634073 | B2 | 19930211 | | |
| ZA 9105466 | A | 19920429 | ZA 1991-5466 | 19910712 |
| HU 59313 | A2 | 19920528 | HU 1991-2359 | 19910712 |
| HU 206973 | B | 19930301 | | |
| IL 98810 | A1 | 19960119 | IL 1991-98810 | 19910712 |
| RU 2070408 | C1 | 19961220 | RU 1991-5001150 | 19910712 |
| CN 1058716 | A | 19920219 | CN 1991-104030 | 19910713 |
| CN 1070700 | B | 20010912 | | |
| KR 182811 | B1 | 19990501 | KR 1991-11967 | 19910713 |
| JP 05032627 | A2 | 19930209 | JP 1991-188472 | 19910729 |
| US 5284861 | A | 19940208 | US 1992-890730 | 19920601 |
| LV 10048 | B | 19950620 | LV 1992-173 | 19921027 |
| LT 3593 | B | 19951227 | LT 1993-919 | 19930903 |
| PRIORITY APPLN. INFO.: | | | DE 1990-4022442 A1 | 19900714 |

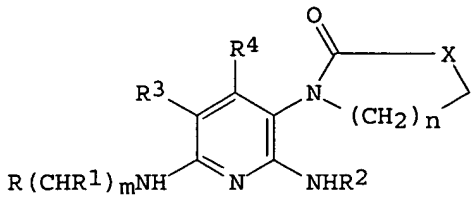
EP 1991-111124 A3 19910704
US 1991-726408 A3 19910710

AB Flupirtine (I) is a spasmolytic for muscles. I may be used for increasing the tonus of skeletal muscles in parkinsonism, optionally in combination with known drugs for the treatment of parkinsonism, such as (-)-deprenyl, biperiden or L-DOPA. I.p. administration of 5 mg I + 5 mg L-DOPA/kg decreased in vivo the reserpine-induced rigidity of the rat flexor muscle.

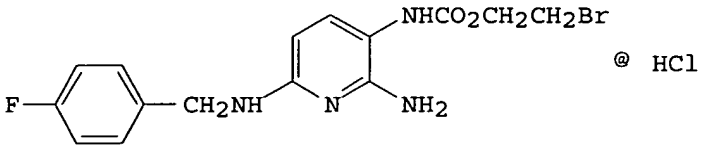
L16 ANSWER 29 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:235286 HCAPLUS
DOCUMENT NUMBER: 112:235286
TITLE: Preparation of (aminopyridyl)oxazolidinones and their analogs as antiepileptics
INVENTOR(S): Engel, Juergen; **Emig, Peter**; Nickel, Bernd; Szelenyi, Istvan
PATENT ASSIGNEE(S): Asta Pharma A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3915184 | A1 | 19891130 | DE 1989-3915184 | 19890510 |
| EP 343429 | A1 | 19891129 | EP 1989-108369 | 19890510 |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| DK 8902326 | A | 19891117 | DK 1989-2326 | 19890512 |
| AU 8934819 | A1 | 19891116 | AU 1989-34819 | 19890515 |
| JP 02017186 | A2 | 19900122 | JP 1989-120578 | 19890516 |
| US 4923858 | A | 19900508 | US 1989-352287 | 19890516 |

PRIORITY APPLN. INFO.: DE 1988-3816629 A1 19880516
OTHER SOURCE(S): CASREACT 112:235286; MARPAT 112:235286
GI




I




@ HCl

II

AB The title compds. [I; R = (substituted) aryl; R1, R2 = H, alkyl; R3, R4 = H, alkyl, OH, alkoxy, etc.; X = O, S, (substituted) imino; m, n = 1, 2, 3] are prepared Bromoethyl pyridylcarbamate II in EtOH was treated with NH3 in EtOH at room temperature for 24 h to give I [R = p-FC6H4, R1-R4 = H, X = O, m = n = 1]. In an example using the maximum elec. shock test, the ED50 for I (no specific compound mentioned) was 56 mg/kg in mice. Capsules and

suppositories containing I were formulated.

L16 ANSWER 30 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:453587 HCAPLUS
DOCUMENT NUMBER: 111:53587
TITLE: Determination of total bilirubin in serum and test strip determination for bilirubinemia, urobilinogenuria, and proteinuria: interference form the analgesic flupirtin
AUTHOR(S): Thomas, L.; Riethmueller-Winzen, H.; Niebch, G.; **Emig, P.**; Harleman, J. H.
CORPORATE SOURCE: Zentrallab., Krankenhaus Nordwest, Frankfurt/Main, D-6900/90, Fed. Rep. Ger.
SOURCE: Laboratoriumsmedizin (1989), 13(4), 136-41
CODEN: LABOD3; ISSN: 0342-3026
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Test strips (Ames-N-multistix, Combur-9-Test, Rapignost-Total-Screen) gave false-pos. results for bilirubin (I), urobilinogen (II), and protein (III) detns. in human urine in the presence of flupirtine (IV), either following in vitro spiking of samples or after daily oral administration of the drug to patients. For I and II detns., strongly colored azo-type reactions with the indicator reagents were observed; for III detns. the reason for this interference was not found, although expts. indicated that the biuret determination of III was not influenced by IV. Test-strip detns. of total blood serum I were also influenced by IV (i.e. they indicated increased I values in a IV dose-dependent manner) which depended upon assay system used, but at the maximum serum levels of IV expected, this interference was clin. insignificant.

L16 ANSWER 31 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:492815 HCAPLUS
DOCUMENT NUMBER: 109:92815
TITLE: Preparation of 2,6-diamino-3-(halobenzyl)pyridines as analgesics and antipyretics
INVENTOR(S): **Emig, Peter**; Engel, Juergen; Scheffler, Gerhard; Weischer, Carl Heinrich; Nickel, Bernd
PATENT ASSIGNEE(S): Asta Pharma A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3637829 | A1 | 19880511 | DE 1986-3637829 | 19861106 |
| CN 87106966 | A | 19880831 | CN 1987-106966 | 19871019 |
| EP 266711 | A1 | 19880511 | EP 1987-116036 | 19871031 |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| FI 8704875 | A | 19880507 | FI 1987-4875 | 19871104 |
| DD 270903 | A5 | 19890816 | DD 1987-308667 | 19871104 |
| DD 276280 | A5 | 19900221 | DD 1987-323143 | 19871104 |
| PL 149462 | B1 | 19900228 | PL 1987-268592 | 19871104 |
| DK 8705814 | A | 19880507 | DK 1987-5814 | 19871105 |
| NO 8704617 | A | 19880509 | NO 1987-4617 | 19871105 |
| AU 8780826 | A1 | 19880512 | AU 1987-80826 | 19871105 |
| AU 596708 | B2 | 19900510 | | |

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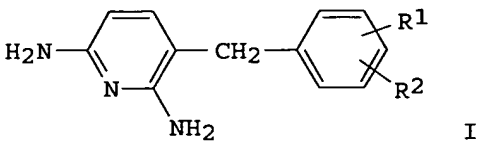
|---|---|---|---|---|
| JP 63132875 | A2 | 19880604 | JP 1987-278411 | 19871105 |
| ZA 8708324 | A | 19880629 | ZA 1987-8324 | 19871105 |
| HU 45502 | A2 | 19880728 | HU 1987-4965 | 19871105 |
| HU 197882 | B | 19890628 | | |
| US 4851420 | A | 19890725 | US 1987-116807 | 19871105 |

PRIORITY APPLN. INFO.: DE 1986-3637829 A 19861106
OTHER SOURCE(S): CASREACT 109:92815; MARPAT 109:92815
GI



I

AB The title compds. (I; R1 = F; R2 = H, Cl) were prepared as analgesics and antipyretics (no data). 2,6-Diaminopyridine was slowly heated to melting and 4-FC6H4CH2Cl was added dropwise followed by heating at 130-150° for 4 h to give 59% 2,6-diamino-3-(4-fluorobenzyl)pyridine.

L16 ANSWER 32 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:50057 HCAPLUS
DOCUMENT NUMBER: 106:50057
TITLE: 2-Amino-3-nitro-6-(4-fluorobenzylamino)pyridine and 2-amino-3-carbethoxyamino-6-(4-fluorobenzylamino)pyridine
INVENTOR(S): Orth, Winfried; Engel, Juergen; **Emig, Peter**; Scheffler, Gerhard; Pohle, Hans
PATENT ASSIGNEE(S): Degussa A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3608762 | A1 | 19861002 | DE 1986-3608762 | 19860315 |
| NO 8600825 | A | 19860924 | NO 1986-825 | 19860305 |
| EP 199951 | A2 | 19861210 | EP 1986-103517 | 19860315 |
| EP 199951 | A3 | 19871014 | | |
| EP 199951 | B1 | 19910123 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| AT 60322 | E | 19910215 | AT 1986-103517 | 19860315 |
| DK 8601268 | A | 19860924 | DK 1986-1268 | 19860319 |
| DK 162215 | B | 19910930 | | |
| DK 162215 | C | 19920316 | | |
| FI 8601183 | A | 19860924 | FI 1986-1183 | 19860320 |
| FI 84819 | B | 19911015 | | |
| FI 84819 | C | 19920127 | | |
| AU 8654997 | A1 | 19860925 | AU 1986-54997 | 19860321 |
| AU 579922 | B2 | 19881215 | | |
| ZA 8602138 | A | 19861126 | ZA 1986-2138 | 19860321 |
| BR 8601283 | A | 19861202 | BR 1986-1283 | 19860321 |
| ES 553222 | A1 | 19870116 | ES 1986-553222 | 19860321 |
| DD 246761 | A5 | 19870617 | DD 1986-288169 | 19860321 |

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|---|---|---|---|---|---|
| CS 259887 | B2 | 19881115 | CS 1986-1986 | | 19860321 |
| PL 146631 | B1 | 19890228 | PL 1986-258543 | | 19860321 |
| IL 78218 | A1 | 19891215 | IL 1986-78218 | | 19860321 |
| CA 1273343 | A1 | 19900828 | CA 1986-504732 | | 19860321 |
| JP 61221172 | A2 | 19861001 | JP 1986-64292 | | 19860324 |
| JP 01046510 | B4 | 19891009 | | | |
| HU 40418 | A2 | 19861228 | HU 1986-1216 | | 19860324 |
| HU 206679 | B | 19921228 | | | |
| US 4785110 | A | 19881115 | US 1986-843253 | | 19860324 |
| PRIORITY APPLN. INFO.: | | | DE 1985-3510623 | A1 | 19850323 |
| | | | EP 1986-103517 | A | 19860315 |

OTHER SOURCE(S): CASREACT 106:50057

AB The title compds. (I and II resp.) were prepared Thus, 25-amino-3-nitro-6-methoxy-pyridine was condensed with 4-FC6H4CH2NH2 to give 95.2% I. I (26.2 g) was reduced with Raney-Ni in dioxane and acylated with ClCO2Et to give 19 g II.

L16 ANSWER 33 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:632448 HCAPLUS
DOCUMENT NUMBER: 105:232448
TITLE: Preparation of flupirtine gluconate salt for injection
INVENTOR(S): Hettche, Helmut; **Emig, Peter**; Engel, Juergen
PATENT ASSIGNEE(S): Degussa A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| DE 3416609 | A1 | 19851107 | DE 1984-3416609 | | 19840505 |
| EP 160865 | A2 | 19851113 | EP 1985-104746 | | 19850419 |
| EP 160865 | A3 | 19860312 | | | |
| EP 160865 | B1 | 19880420 | | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | | |
| AT 33638 | E | 19880515 | AT 1985-104746 | | 19850419 |
| SU 1398772 | A3 | 19880523 | SU 1985-3884101 | | 19850426 |
| CS 248743 | B2 | 19870212 | CS 1985-3157 | | 19850430 |
| US 4673666 | A | 19870616 | US 1985-729413 | | 19850501 |
| DK 8501987 | A | 19851106 | DK 1985-1987 | | 19850502 |
| DK 157016 | B | 19891030 | | | |
| DK 157016 | C | 19900326 | | | |
| DD 236927 | A5 | 19860625 | DD 1985-275890 | | 19850502 |
| FI 8501752 | A | 19851106 | FI 1985-1752 | | 19850503 |
| FI 80443 | B | 19900228 | | | |
| FI 80443 | C | 19900611 | | | |
| NO 8501772 | A | 19851106 | NO 1985-1772 | | 19850503 |
| AU 8541943 | A1 | 19851107 | AU 1985-41943 | | 19850503 |
| ES 542817 | A1 | 19851216 | ES 1985-542817 | | 19850503 |
| ZA 8503351 | A | 19851224 | ZA 1985-3351 | | 19850503 |
| HU 37758 | A2 | 19860228 | HU 1985-1691 | | 19850503 |
| HU 193753 | B | 19871130 | | | |
| IL 75086 | A1 | 19880331 | IL 1985-75086 | | 19850503 |
| CA 1263398 | A1 | 19891128 | CA 1985-480723 | | 19850503 |
| JP 60239469 | A2 | 19851128 | JP 1985-95714 | | 19850507 |
| JP 01044185 | B4 | 19890926 | | | |
| PRIORITY APPLN. INFO.: | | | DE 1984-3416609 | A | 19840505 |
| | | | EP 1985-104746 | A | 19850419 |

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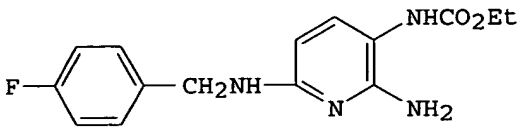


I

AB Flupirtine (I) gluconate salt is prepared by reacting I with gluconic acid or gluconic acid-δ-lactone to improve its solubility and stability. A parenteral solution can be formulated using solvents such as polyethylene glycol, glycofurol, and water. Thus I was added to a solution of gluconic acid obtained by hydrolysis of gluconic acid-δ-lactone. A mixture containing I gluconate salt, PEG, and NaHSO3 was microfiltered and stored in colorless ampules.

L16 ANSWER 34 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:610967 HCAPLUS
DOCUMENT NUMBER: 101:210967
TITLE: Ethylenediamine and guanidine derivatives
INVENTOR(S): **Emig, Peter**; Scheffler, Gerhard; Thiemer, Klaus; Weischer, Carl Heinrich
PATENT ASSIGNEE(S): Degussa A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3343884 | A1 | 19840614 | DE 1983-3343884 | 19831205 |
| DE 3343884 | C2 | 19910711 | | |
| NL 8303965 | A | 19840702 | NL 1983-3965 | 19831117 |
| SU 1222196 | A3 | 19860330 | SU 1983-3663583 | 19831121 |
| FR 2537582 | A1 | 19840615 | FR 1983-19390 | 19831205 |
| FR 2537582 | B1 | 19861205 | | |
| BE 898403 | A1 | 19840606 | BE 1983-47911 | 19831206 |
| AU 8322138 | A1 | 19840614 | AU 1983-22138 | 19831206 |
| AU 564254 | B2 | 19870806 | | |
| GB 2132615 | A1 | 19840711 | GB 1983-32433 | 19831206 |
| GB 2132615 | B2 | 19860702 | | |
| DD 216013 | A5 | 19841128 | DD 1983-257557 | 19831206 |
| DK 8305633 | A | 19840609 | DK 1983-5633 | 19831207 |
| DK 163732 | B | 19920330 | | |
| DK 163732 | C | 19920831 | | |
| FI 8304481 | A | 19840609 | FI 1983-4481 | 19831207 |
| SE 8306764 | A | 19840609 | SE 1983-6764 | 19831207 |
| ZA 8309107 | A | 19840725 | ZA 1983-9107 | 19831207 |
| ES 527864 | A1 | 19840801 | ES 1983-527864 | 19831207 |
| HU 35255 | O | 19850628 | HU 1983-4192 | 19831207 |
| IL 70401 | A1 | 19871030 | IL 1983-70401 | 19831207 |
| US 4738983 | A | 19880419 | US 1983-558984 | 19831207 |
| CA 1257867 | A1 | 19890725 | CA 1983-442695 | 19831207 |
| AT 8304278 | A | 19900115 | AT 1983-4278 | 19831207 |
| AT 390952 | B | 19900725 | | |

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|---|---|---|---|---|
| JP 59112980 | A2 | 19840629 | JP 1983-230710 | 19831208 |
| JP 05072386 | B4 | 19931012 | | |
| CS 241141 | B2 | 19860313 | CS 1983-9224 | 19831208 |
| CH 657850 | A | 19860930 | CH 1983-6576 | 19831208 |
| PRIORITY APPLN. INFO.: | | | DE 1982-3245387 | A1 19821208 |
| OTHER SOURCE(S): | MARPAT 101:210967 | | | |

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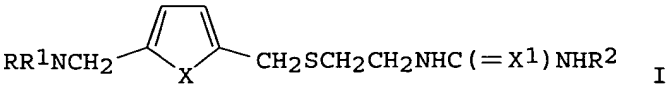

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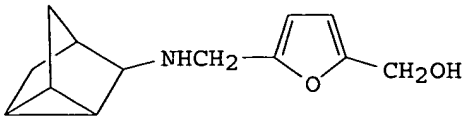


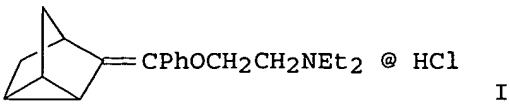
II

AB The title compds. [I; R = polycycloalkyl, (un)substituted alkyl, cycloalkyl; R1 = H, (un)substituted alkyl; R2 = H, alkenyl, alkynyl, cycloalkyl, 2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl, (un)substituted alkyl; X = O, S; X1 = R3CH, RN; R3 = NO2, cyano] were prepared Thus, 2-furanmethanol was aminomethylated with R4NH2 (R4 = tricyclo[2.2.1.22,6]hept-3-yl] and paraformaldehyde to give II, which was condensed with HSCH2CH2NH.HCl, O2NC:C(SMe)2 and MeNH2 to give I (R = R4, R1 = H, R2 = Me, X = O, X1 = O2NCH). I are as effective as ranitidine in inhibiting stomach secretion in rats.

L16 ANSWER 35 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1983:143000 HCAPLUS |
| DOCUMENT NUMBER: | 98:143000 |
| TITLE: | Synthesis and structure of new basic enol ethers |
| AUTHOR(S): | Risch, N.; **Emig, P.**; Scheffler, G.; Pohle, H.; Henkel, G. |
| CORPORATE SOURCE: | Forsch. Geschaeftsber. Pharma, Degussa A.-G., Frankfurt/Main, Fed. Rep. Ger. |
| SOURCE: | Arzneimittel-Forschung (1982), 32(11), 1409-11 CODEN: ARZNAD; ISSN: 0004-4172 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | German |
| OTHER SOURCE(S): | CASREACT 98:143000 |

GI



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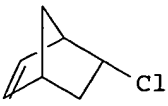

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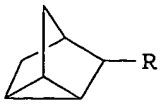

III

AB Enol ethers (E)- and (Z)-I are spasmolytics and also have antiallergy and antidepressant properties. Treating bicyclo[2.2.1]hepta-2,5-diene in CH2Cl2 with HCl(g) 6 h gave 88.2% a mixture of II and III (R = Cl). Grignard reaction of the mixture gave III [R = PhC(:NH)], hydrolysis of which gave 93.8% III (R = Bz). This, with NaNH2 and Et2NCH2CH2Cl in refluxing PhMe gave 81.7% free base, which was converted to I. X-ray anal. of (E)-I confirmed the structure.

L16 ANSWER 36 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:89707 HCAPLUS
DOCUMENT NUMBER: 84:89707
TITLE: Basic enol ethers and their salts
INVENTOR(S): **Emig, Peter**; Pohle, Hans; Scheffler, Gerhard; Brock, Norbert; Lenke, Hans D.; Pohl, Joerg
PATENT ASSIGNEE(S): Asta-Werke A.-G. Chemische Fabrik, Fed. Rep. Ger.
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2413814 | A1 | 19751002 | DE 1974-2413814 | 19740322 |
| DE 2413814 | C3 | 19791004 | | |
| DE 2413814 | B2 | 19790201 | | |
| CH 610291 | A | 19790412 | CH 1975-2745 | 19750305 |
| SE 7502607 | A | 19750923 | SE 1975-2607 | 19750307 |
| SE 421916 | B | 19820208 | | |
| SE 421916 | C | 19820527 | | |
| ZA 7501415 | A | 19760526 | ZA 1975-1415 | 19750307 |
| IL 46786 | A1 | 19771130 | IL 1975-46786 | 19750310 |
| US 4065501 | A | 19771227 | US 1975-557535 | 19750312 |
| AU 7579012 | A1 | 19760916 | AU 1975-79012 | 19750313 |
| GB 1446164 | A | 19760818 | GB 1975-10992 | 19750317 |
| DD 119208 | C | 19760412 | DD 1975-184851 | 19750318 |
| AT 7502073 | A | 19770315 | AT 1975-2073 | 19750318 |
| AT 339878 | B | 19771110 | | |
| CS 185682 | P | 19781031 | CS 1975-1816 | 19750318 |
| CS 185698 | P | 19781031 | CS 1977-914 | 19750318 |
| CA 1054152 | A1 | 19790508 | CA 1975-222446 | 19750318 |
| DK 7501111 | A | 19750923 | DK 1975-1111 | 19750319 |
| DK 141818 | B | 19800623 | | |
| DK 141818 | C | 19801110 | | |
| JP 50129539 | A2 | 19751013 | JP 1975-33471 | 19750319 |
| JP 58029777 | B4 | 19830624 | | |
| FR 2264523 | A1 | 19751017 | FR 1975-8742 | 19750320 |
| FR 2264523 | B1 | 19790629 | | |
| ES 435796 | A1 | 19761216 | ES 1975-435796 | 19750320 |
| PL 97364 | P | 19780228 | PL 1975-178944 | 19750320 |
| PL 97365 | P | 19780228 | PL 1975-195370 | 19750320 |
| BE 826950 | A1 | 19750716 | BE 1975-2054220 | 19750321 |
| FI 7500856 | A | 19750923 | FI 1975-856 | 19750321 |
| FI 62662 | B | 19821029 | | |
| FI 62662 | C | 19830210 | | |
| NL 7503414 | A | 19750924 | NL 1975-3414 | 19750321 |
| SU 614743 | D | 19780705 | SU 1975-2115295 | 19750321 |
| HU 173792 | P | 19790828 | HU 1975-AA807 | 19750321 |

| | | | | | |
|---|---|---|---|---|---|
| AT 7606966 | A | 19770215 | AT 1976-6966 | | 19760920 |
| AT 339278 | B | 19771010 | | | |
| SU 639444 | D | 19781225 | SU 1977-2440657 | | 19770124 |
| US 4124716 | A | 19781107 | US 1977-842092 | | 19771014 |
| PRIORITY APPLN. INFO.: | | | DE 1974-2413814 | A | 19740322 |
| | | | US 1975-557535 | A2 | 19750312 |
| | | | AT 1975-2073 | A | 19750318 |

OTHER SOURCE(S): MARPAT 84:89707
GI For diagram(s), see printed CA Issue.
AB The enol ethers I (R = Ph, substituted phenyl, thienyl, pyridyl; R1 = H, Me, Et; R2 = Me, Et; NR1R2 = pyrrolidino, morpholino; n = 2,3), useful as spasmolytics were prepared Thus, II and Me2NCH2CH2Cl were added to a suspension of NaNH2 in boiling PhMe, and the mixture was refluxed for 1.5 hr to give 76% I (R = Ph, R1 = R2 = Me, n = 2). About 15 I were prepared and tested for spasmolytic activity on guinea pigs.

L16 ANSWER 37 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1970:477580 HCAPLUS
DOCUMENT NUMBER: 73:77580
TITLE: Nucleosides. X. Synthesis of dipeptidyl aminosugar nucleosides structurally related to gougerotin
AUTHOR(S): Lichtenthaler, Frieder W.; Trummlitz, G.; **Emig, Peter**
CORPORATE SOURCE: Inst. Org. Chem., Tech. Hochsch., Darmstadt, Fed. Rep. Ger.
SOURCE: Tetrahedron Letters (1970), (24), 2061-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB N-tert-Butoxycarbonylsarcosine, prepared from sarcosine and 2,4,5-Cl3C6H2O2COBu-tert, was treated with D-serine Me ester-HCl to give N-tert-butoxycarbonylsarcosyl-D-serine Me ester which was converted into the corresponding hydrazide. The latter treated with BuNO2 in DMF gave the corresponding azide which was coupled with 1-(3-amino-3-deoxy-β-D-glucopyranosyl)cytosine (Luebke, K., et al., 1964) to give a tert-butoxycarbonyl-blocked dipeptidyl nucleoside which on removal of the protecting group with F3CCO2H gave 1-[3-(sarcosyl-D-serylamido)-3-deoxy-β-D-glucopyranosyl]cytosine (I). Similarly prepared was II.

L16 ANSWER 38 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:106817 HCAPLUS
DOCUMENT NUMBER: 70:106817
TITLE: Nucleosides. VIII. Configuration assignment of sugars and hexopyranosyl nucleosides by the acetyl-resonance rule
AUTHOR(S): Lichtenthaler, Frieder W.; Bambach, Gerd; **Emig, Peter**
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1969), 102(3), 994-1004
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The 1H N.M.R. spectra were recorded for per-O-acetyl-D-aldopyranoses and the corresponding per-O-acetyl-2-amino-2-deoxy-D-aldopyranoses with per-O-D-gluco, D-galacto, and D-manno configurations in CDCl3 and (D3C)2SO. Results are tabulated and solvents shifts were determined Solvent shifts of the Ac protons were small (≤0.05 ppm.) in comparison with diamagnetic solvent shifts, .apprx.0.15 ppm., of the NHAc group. In fully acetylated hexopyranosyl nucleosides, the anisotropy of the base causes a

acetamido groups.

L16 ANSWER 41 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:454388 HCAPLUS
DOCUMENT NUMBER: 67:54388
TITLE: N.M.R. studies on sugars and cyclanols. III. Configuration of C-methyl-branched sugars and cyclanols at the branching point
AUTHOR(S): Lichtenthaler, Frieder W.; **Emig, P.**
CORPORATE SOURCE: Tech. Hochsch., Darmstadt, Fed. Rep. Ger.
SOURCE: Tetrahedron Letters (1967), (7), 577-82
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. CA 64: 19740c. Summary of N.M.R. studies of peracetates of sugars, cyclanols, amino sugars, and amino-cyclanols in $CDCl_3$ showed that the signal positions of acetoxy and acetamido resonances offer a convenient and generally surprisingly accurate means for configurational and conformational assignments. In view of this relationship similar relations would be expected for CMeOAc and CMeNHAc groups. In a summary of the chemical shifts in $CDCl_3$ of δ C-Me branched cyclanol acetates the differences in chemical shift between the equatorial and axial C-Me protons was small. However, the Me protons of the AcO group at the branching point showed differences of about 0.1 ppm. between axial and equatorial orientation showing the replacement of a ring H atom by a Me group causes an upward shift of the AcO signal. Accordingly, the configuration at the branching point can be deduced from the signal position of the AcO group attached to the C-Me branch of a cyclanol. A similar upward shift can be assumed for the Me protons of acetamido groups when an Me group is substituted for the ring H atom. The expected range for axial C-Me acetamido groups would thus be 8.07-8.14 τ as compared with 8.13-8.22 τ for their equatorial counterparts. Of the 7 C-Me branched aminocyclanol and amino sugar acetates which have been prepared and whose configuration at the branching point had not been assigned, the acetamido signals appear within the very small range of 0.05 ppm. and on the basis of their chemical shifts (8.15-8.20 τ) indicated an equatorial acetamido group in each compound and permitted the configurational assignments given. Since all compds. were prepared by cyclization of a dialdehyde with $EtNO_2$, it was concluded that the $EtNO_2$ cyclization proceeds analogous to the $MeNO_2$-dialdehyde cyclization, with the $NO_2$ group preferentially, if not exclusively, attaining the equatorial position in the cyclization step.

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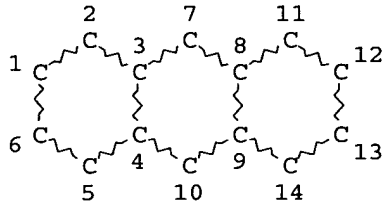
L5 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

general diamagnetic shift of the vicinal 2'-acetyl signals: 0.1 ppm. for pyrimidine; 0.3 ppm. for purine. Configurations of the hexopyranosyl nucleosides were thus unambiguously determined

L16 ANSWER 39 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:106813 HCAPLUS
DOCUMENT NUMBER: 70:106813
TITLE: Nucleosides. VI. Nucleoside conversion in the 3'-aminohexosyl-hypoxanthine series
AUTHOR(S): Lichtenthaler, Frieder W.; **Emig, Peter**; Bommer, Dieter
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1969), 102(3), 971-85
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Cyclization of 2-O-[(R)-formyl(hypoxanthin-9-yl)methyl]-D-glyceraldehyde with MeNO2 yielded 9-(3-deoxy-3-nitro-β-D-glucopyranosyl)hypoxanthine and 9-(3-deoxy-3-nitro-β-D-galactopyranosyl)hypoxanthine. The latter gave upon hydrogenation 9-(3-amino-3-deoxy-β-D-galactopyranosyl)hypoxanthine. 9-(3-Acetamido-4,6-O-benzylidene - 3 - deoxy - β - D -glucopyranosyl)hypoxanthine was converted into its 2-O-(methylsulfonyl) derivative which heated with NaOAc gave 9-(3-acetamido-4,6-O-benzylidene-3-deoxy-β-D-mannopyranosyl)hypoxanthine. The latter was acetylated, after the removal of the 4,6-O-benzylidene group, to give 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-mannopyranosyl)hypoxanthine. Similarly was prepared 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-talopyranosyl)hypoxanthine, starting from 9-(3-acetamido)-4,6-O-benzylidene-3-deoxy-β-D-galactopyranosyl)hypoxanthine. Treatment of 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-glucopyranosyl)hypoxanthine with P4S10 in pyridine gave 9-(2,4,6-tri-O-acetyl-3-deoxy-3-thioacetamido-β-D-glucopyranosyl)hypoxanthine and 6-mercapto-9-(2,3,6-tri-O-acetyl-3-deoxy-3-thioacetamido-β-D-glucopyranosyl)purine (I). I was converted into the corresponding 6-(methylthio) derivative which upon ammonolysis, followed by acetylation, gave 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-glucopyranosyl)adenine. The chlorination of I, followed by the addition of Me2NH gave 9-(3-acetamido-3-deoxy-β-D-glucopyranosyl)-6-(dimethylamino)purine.

L16 ANSWER 40 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:444143 HCAPLUS
DOCUMENT NUMBER: 69:44143
TITLE: Nuclear magnetic resonance studies on sugars and cyclanols. V. Relation between the steric orientation of O- and N-acetyl groups and the methyl resonance signal location in cyclitol and aminocyclitol polyacetates
AUTHOR(S): Lichtenthaler, F. W.; **Emig, P.**
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, Fed. Rep. Ger.
SOURCE: Carbohydrate Research (1968), 7(2), 121-37
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Absorption ranges are deduced for axial and equatorial O-and N-acetyl-resonances of cyclitol and aminocyclitol peracetates on the basis of 41 (CDCl3) and 22 (Me2SO-d6) compds., allowing configurational and conformational assignments. Scope and limitations are discussed; especially application to compds. having substituents other than acetoxy and

RSPEC I
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
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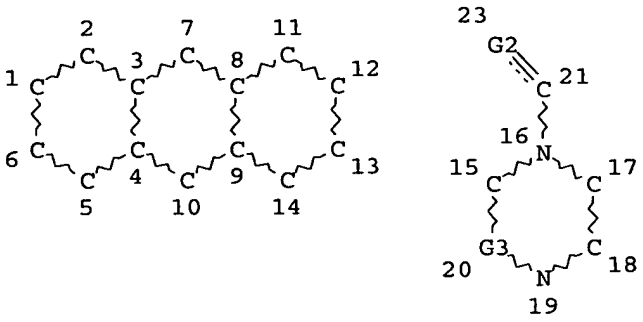
L8 STR




VAR G2=O/S
REP G3=(1-4) C
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 16
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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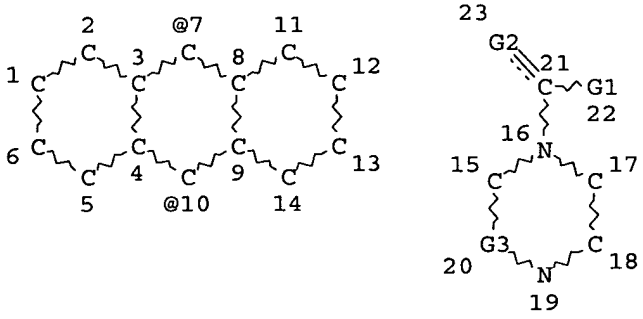


VAR G1=7/10
VAR G2=O/S
REP G3=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 15
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
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L12 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
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PETER"/AU)
L16 41 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 NOT L12
L17 67 SEA FILE=HCAPLUS ABB=ON PLU=ON ("GUNTHER E"/AU OR "GUNTHER ECKHARD"/AU) NOT (L12 OR L16)

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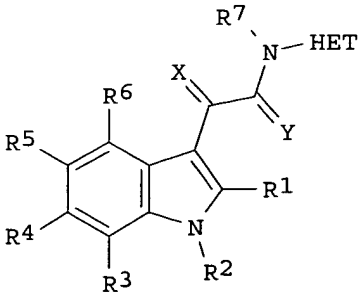
L17 ANSWER 1 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:78242 HCAPLUS
DOCUMENT NUMBER: 142:176683
TITLE: Preparation of N-substituted indolyl-3-glyoxylamides as antitumor agents
INVENTOR(S): Gerlach, Matthias; Schuster, Tilmann; Schmidt, Peter; Baasner, Silke; **Gunther, Eckhard**
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2005020636 | A1 | 20050127 | US 2004-892040 | | 20040715 |
| PRIORITY APPLN. INFO.: | | | US 2003-490004P | P | 20030725 |

OTHER SOURCE(S): MARPAT 142:176683
GI

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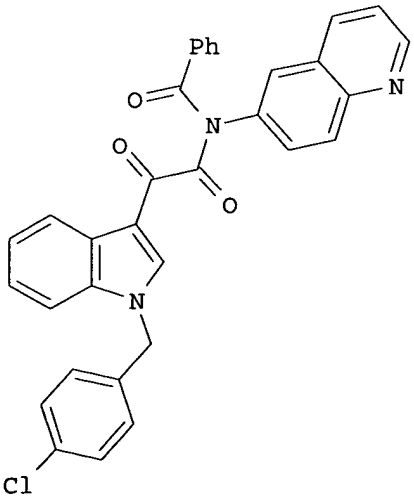



II

AB The title compds. I [R1, R3-R6 = H, (un)substituted (cyclo)alkyl, (hetero)aryl, alkylaryl, etc.; R2 = (un)substituted alkyl, alkylaryl, alkylheteroaryl; R7 = SO2X1 (wherein X1 = dialkylamino, OH, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.), COX2 (X2 = (un)substituted (hetero)aryl, alkylaryl, alkylheteroaryl), etc.; X = O, S or geminally linked H and OH; Y = O, S; HET = (un)saturated or aromatic

heterocycle comprising N, O and S which can be bonded to the amide nitrogen directly or via alkyl bridge], useful as medicaments, in particular for the treatment of tumors, were prepared General procedure for synthesis of compds. I such as II which comprises reacting 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-quinolin-6-ylacetamide with acyl chloride, was described. The compound II was tested for inhibition of selected tumor cell lines and antiproliferative action on MDR tumor cell lines (data given). The pharmaceutical composition comprising the compound I is disclosed.

L17 ANSWER 2 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:252340 HCAPLUS
DOCUMENT NUMBER: 140:264487
TITLE: Medicaments containing disorazoles and derivatives thereof for the treatment of benign and malignant tumors
INVENTOR(S): Irschik, Herbert; Jansen, Rolf; Sasse, Florenz; Baasner, Silke; Schmidt, Peter; **Gunther, Eckhard**
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2004024149 | A1 | 20040325 | WO 2003-EP9329 | | 20030822 |
| W: AT, AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA | | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | | | |
| CA 2438001 | AA | 20040224 | CA 2003-2438001 | | 20030822 |
| AU 2003296872 | A1 | 20040430 | AU 2003-296872 | | 20030822 |
| US 2004106662 | A1 | 20040603 | US 2003-646904 | | 20030822 |
| EP 1536789 | A1 | 20050608 | EP 2003-794920 | | 20030822 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2003013789 | A | 20050705 | BR 2003-13789 | | 20030822 |
| CN 1678310 | A | 20051005 | CN 2003-820093 | | 20030822 |
| JP 2006500398 | T2 | 20060105 | JP 2004-535140 | | 20030822 |
| ZA 2005001196 | A | 20050901 | ZA 2005-1196 | | 20050210 |
| NO 2005001444 | A | 20050519 | NO 2005-1444 | | 20050318 |
| PRIORITY APPLN. INFO.: | | | US 2002-405594P | P | 20020824 |
| | | | WO 2003-EP9329 | W | 20030822 |

OTHER SOURCE(S): MARPAT 140:264487
AB The invention discloses disorazole compds. which are used as medicaments, preferably in the treatment of tumors, especially in the case of drug resistance and in metastasizing carcinoma. Possible uses thereof are not restricted to tumor diseases.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:149217 HCAPLUS

DOCUMENT NUMBER: 141:77736
TITLE: LSC measurements of the half-life of 40K
AUTHOR(S): Kossert, K.; **Gunther, E.**
CORPORATE SOURCE: Department 6.1, Physikalisch-Technische Bundesanstalt, Braunschweig, 38116, Germany
SOURCE: Applied Radiation and Isotopes (2004), 60(2-4), 459-464
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liquid scintillation counting techniques combined with the CIEMAT/NIST method have been applied to measure the specific activity of natural potassium salts. Samples have been prepared with three different scintillators. The individual atomic composition as well as the d. of the cocktails have been taken into account for the efficiency calcn. With the specific activity the half-life is calculated to be T1/2 = 1.248(3) + 109 a. The result is in reasonable agreement with other measurement results provided the same isotopic concentration of 40K is used.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:149215 HCAPLUS
DOCUMENT NUMBER: 141:30008
TITLE: Ionization quenching in LSC
AUTHOR(S): Carles, Grau; **Gunther, E.**; Garcia, G.; Malonda, A. Grau
CORPORATE SOURCE: CIEMAT, Instituto de Estudios de la Energia, Madrid, 28040, Spain
SOURCE: Applied Radiation and Isotopes (2004), 60(2-4), 447-451
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ionization quench function Q(E) introduces an important correction in the CIEMAT/NIST tracing method. The authors present a detailed anal. of the equations used to compute the counting efficiency of 55Fe. The counting efficiency of this radionuclide is very sensitive to the shape and values of Q(E) for this method. The Birks equation and stopping power are not adequate to obtain low discrepancies between the exptl. and computed efficiencies. An empirical procedure to compute accurate Q(E) functions is also given.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:120730 HCAPLUS
DOCUMENT NUMBER: 140:157434
TITLE: Use of alkyl phosphocholines in combination with antitumor medicaments for the treatment of benign and malignant tumors
INVENTOR(S): Engel, Jurgen; **Gunther, Eckhard**; Sindermann, Herbert
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2004012744 | A1 | 20040212 | WO 2003-EP8346 | | 20030729 |
| W: AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA | | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | | | |
| CA 2493023 | AA | 20040212 | CA 2003-2493023 | | 20030729 |
| AU 2003253350 | A1 | 20040223 | AU 2003-253350 | | 20030729 |
| BR 2003013048 | A | 20050614 | BR 2003-13048 | | 20030729 |
| EP 1545553 | A1 | 20050629 | EP 2003-766336 | | 20030729 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| CN 1671397 | A | 20050921 | CN 2003-818101 | | 20030729 |
| JP 2005535688 | T2 | 20051124 | JP 2004-525354 | | 20030729 |
| US 2004097470 | A1 | 20040520 | US 2003-632187 | | 20030730 |
| CA 2436332 | AA | 20050131 | CA 2003-2436332 | | 20030731 |
| ZA 2005000453 | A | 20050718 | ZA 2005-453 | | 20050118 |
| NO 2005001040 | A | 20050225 | NO 2005-1040 | | 20050225 |
| PRIORITY APPLN. INFO.: | | | US 2002-399615P | P | 20020730 |
| | | | WO 2003-EP8346 | W | 20030729 |

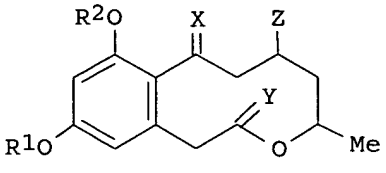
OTHER SOURCE(S): MARPAT 140:157434

AB The invention discloses the use of alkyl phosphocholines in combination with antitumor medicaments for treating benign and malignant tumor diseases in humans and mammals. The alkyl phosphocholines can be used in combination with one or a combination of several approved cytostatics. Compds. of the invention include e.g. perifosine.

L17 ANSWER 6 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:912847 HCAPLUS
DOCUMENT NUMBER: 139:395749
TITLE: Isolation and synthesis of decalactones from Penicillium species and methods for making pharmaceuticals there from
INVENTOR(S): Bringmann, Gerhard; Proksch, Peter; Edrada, Ru Angelie; Heubes, Markus; **Gunther, Eckhard**
PATENT ASSIGNEE(S): Biotecmarin GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003216354 | A1 | 20031120 | US 2002-143596 | 20020509 |
| US 6872747 | B2 | 20050329 | | |
| PRIORITY APPLN. INFO.: | | | US 2002-143596 | 20020509 |

OTHER SOURCE(S): CASREACT 139:395749; MARPAT 139:395749
GI



I

AB A novel class of decalactones I [R1 = H, (un)branched C1-6-alkyl or C1-6-alkyl mono- or multisubstituted by C6-14-aryl, (un)branched carboxy(C1-18-alkyl), (un)branched (C1-6-alkoxy)carbonyl, (un)branched (C1-12-alkyl)carbonyl, C2-6-alkenyl, C2-6-alkynyl, (un)branched cyano(C1-18-alkyl), OCH2Ph, (9-fluorenylmethoxy)carbonyl (Fmoc), CPh3, 2-(4-pyridyl)ethoxycarbonyl (Pyoc), SiPh2Me (DPMS); R2 = R1; X = O, S, NOH, NOR4; Y = O, S; Z = H, OR3 ; R3 = R1; R4 = (un)branched C1-6-alkyl or C1-6-alkyl mono- or multisubstituted by C6-14-aryl, (un)branched carboxy(C1-18-alkyl), (un)branched (C1-6-alkoxy)carbonyl, (un)branched (C1-12-alkyl)carbonyl], and their enantiomers [R, S] or stereoisomers [(R,R), (R,S), (S,S)] or mixts. thereof, and a method for their isolation is disclosed. Thus, xestodecalactone A [(+)-I; R1 = R2 = H, X = Y = O, Z = H] was isolated from fungus of Penicillium sp. found on freshly collected samples of marine sponge Xestospongia exigua. A method for the synthesis of the decalactones I and the use of the decalactones in pharmaceutical compns. is also described. Thus, (±)-I [R1 = R2 = H, X = Y = O, Z = H] was prepared from 3,5-(HO)2C6H3CH2CO2Me and MeC(:O)(CH2)3CO2H via coupling of 3,5-(PhCH2O)2C6H3CH2CO2H with MeC(OH)(CH2)3CO2Me and intramol. acylation of 3,5-(PhCH2O)2C6H3CH2CO2CHM3(CH2)3CO2H, followed by hydrogenolytic debenzylation. The antitumor activity of I (0.003 - 3.16 μg) was determined (no data).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:414842 HCAPLUS
DOCUMENT NUMBER: 139:226932
TITLE: Evariquinone, isoemericellin, and stromemycin from a sponge derived strain of the fungus Emericella variecolor
AUTHOR(S): Bringmann, Gerhard; Lang, Gerhard; Steffens, Stefan; **Gunther, Eckhard**; Schaumann, Karsten
CORPORATE SOURCE: Institut fuer Organische Chemie der Universitaet, Wuerzburg, D-97074, Germany
SOURCE: Phytochemistry (Elsevier) (2003), 63(4), 437-443
CODEN: PYTCAS; ISSN: 0031-9422
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB From a strain of the fungus Emericella variecolor derived from the marine sponge Haliclona valliculata, two new natural products, evariquinone and isoemericellin, were isolated after HPLC-UV, -MS, and -NMR studies of the extract and their structures were elucidated by mass spectrometry and NMR expts. Evariquinone showed antiproliferative activity towards KB and NCI-H460 cells at a concentration of 3.16 μg/mL. Furthermore, the fungus was found to produce the known metabolites stromemycin, shamixanthone, and 7-hydroxyemodin. Chemical degradation, NMR decoupling expts., and spin-system

simulation provided evidence for the double bonds in stromemycin to be all E-configured. ROESY expts. established the monosaccharide moiety to be glucose.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:980623 HCAPLUS
DOCUMENT NUMBER: 139:75039
TITLE: Characterisation of ceramic breeder materials for the helium cooled pebble bed blanket
AUTHOR(S): Piazza, G.; Reimann, J.; **Gunther, E.**; Knitter, R.; Roux, N.; Lulewicz, J. D.
CORPORATE SOURCE: Institute for Nuclear and Energy Technologies, Forschungszentrum Karlsruhe, Karlsruhe, 76021, Germany
SOURCE: Journal of Nuclear Materials (2002), 307-311(Pt. A), 811-816
CODEN: JNUMAM; ISSN: 0022-3115
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the European He cooled pebble bed (HCPB) blanket slightly hyperstoichiometric Li orthosilicate (Li4SiO4+SiO2) and Li metatitanate (Li2TiO3+TiO2) pebbles are considered as candidate ceramic breeder materials. Such ceramic breeder pebbles and pebble beds were studied in different types of expts. carried out at Forschungszentrum Karlsruhe. In longterm annealing expts. (96 days at 970° in He+0.1% H2 atmosphere) the behavior of the pebbles under DEMO blanket relevant conditions was studied. Mech. uniaxial and triaxial compression tests at temps. up to .apprx.850° were performed to determine the mech. behavior of pebble beds as a function of temperature (stress-strain dependence, thermal creep behavior, friction coeffs.). Thermal conductivity measurements up to .apprx.800° were carried out with the aim to study the effect of creep on the pebble bed heat conduction. An overview of the exptl. activities on ceramic breeder materials is given.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:589583 HCAPLUS
DOCUMENT NUMBER: 137:176626
TITLE: Probing dust around brown dwarfs. The naked LP 944-20 and the disk of Chamaeleon Hα 2
AUTHOR(S): Apai, D.; Pascucci, I.; Henning, Th.; Sterzik, M. F.; Klein, R.; Semenov, D.; **Gunther, E.**; Stecklum, B.
CORPORATE SOURCE: Astrophysikalisches Institut und Universitats-Sternwarte, Jena, D-07745, Germany
SOURCE: Astrophysical Journal (2002), 573(2, Pt. 2), L115-L117
CODEN: ASJOAB; ISSN: 0004-637X
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We present the 1st mid-IR (MIR) detection of a field brown dwarf (BD) and the 1st ground-based MIR measurements of a disk around a young BD candidate. We prove the absence of warm dust surrounding the field BD LP 944-20. In the case of the young BD candidate Cha Hα 2, we find clear evidence for thermal dust emission from a disk. Surprisingly, the object does not exhibit any silicate feature as previously predicted. We show that the flat spectrum can be explained by an optically thick flat

dust disk.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:1269 HCAPLUS
DOCUMENT NUMBER: 136:209711
TITLE: What can we expect from the CIEMAT/NIST method?
AUTHOR(S): **Gunther, E.**
CORPORATE SOURCE: Physikalisch-Technische Bundesantalt (PTB), Braunschweig, 38116, Germany
SOURCE: Applied Radiation and Isotopes (2002), 56(1-2), 357-360
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During the last years the CIEMAT/NIST (C/N) method was widely used to determine activities of different radionuclides. The impression is given that the C/N method could be a universal method for all types of radionuclides. This paper shows under which conditions the C/N method can be used, where its limits are and which uncertainties can typically be achieved.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:1258 HCAPLUS
DOCUMENT NUMBER: 136:407005
TITLE: Determination of the 32P activity in angioplastic balloons by LSC
AUTHOR(S): **Gunther, E.**
CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, 38116, Germany
SOURCE: Applied Radiation and Isotopes (2002), 56(1-2), 291-293
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The determination of the 32P activity in angioplastic balloons involves two problems: the extraction of 32P, which is covered with plastic foils, and the determination of the 33P impurity. At PTB the active balloons are destroyed by combustion in an oxygen stream. The active phosphorus is extracted quant. from the tube. The activities of 32P and 33P are determined by measurements performed over a period of one month or more by a subsequent data fit.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:906962 HCAPLUS
DOCUMENT NUMBER: 137:74215
TITLE: Genomic analysis of MIC genes in rhesus macaques
AUTHOR(S): Seo, J. W.; Walter, L.; **Gunther, E.**
CORPORATE SOURCE: Abteilung Immungenetik, Georg-August-Universitat, Gottingen, D-37073, Germany
SOURCE: Tissue Antigens (2001), 58(3), 159-165
CODEN: TSANA2; ISSN: 0001-2815
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB MIC genes map to the major histocompatibility complex (MHC) and are distantly related to MHC class I genes. Recently, MICA/MICB-like genes have been described in nonhuman primates. In Macaca mulatta, three MICA/B-like genes could be identified: Mamu-MIC1, Mamu-MIC2, and Mamu-MIC3. We show here the isolation and characterization of rhesus macaque cosmid clones which carry the Mamu-MIC2 and Mamu-MIC3 genes. Neither the MIC2- and MIC3-coding sequences nor resp. flanking sequences can be aligned unambiguously to either the human HLA-MICA or -MICB subregions, although MIC2 was found at a similar distance to the BAT1 gene as known for MICB in human. Thus, the characteristics allowing for a classification of primate MIC genes as being of the MICA or MICB types appear to have evolved after the separation of humans and rhesus monkeys from a common ancestor. Furthermore, also Mamu-MICD-containing cosmids could be isolated. In contrast to Mamu-MIC2 and Mamu-MIC3, the Mamu-MICD gene and its flanking sequences are highly conserved and orthologous to the human MICD subregion.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:894716 HCAPLUS
DOCUMENT NUMBER: 136:125154
TITLE: Behaviour of ceramic breeder materials in long time annealing experiments
AUTHOR(S): Piazza, G.; Reimann, J.; **Gunther, E.**; Knitter, R.; Roux, N.; Lulewicz, J. D.
CORPORATE SOURCE: IKET, Forschungszentrum Karlsruhe, Karlsruhe, D-76021, Germany
SOURCE: Fusion Engineering and Design (2001), 58-59, 653-659
CODEN: FEDEEE; ISSN: 0920-3796
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the development of the European Helium Cooled Pebble Bed (HCPB) blanket the reference material is slightly overstoichiometric lithium orthosilicate ($Li_4SiO_4+SiO_2$) pebbles, fabricated by the melting-spraying method. Slightly overstoichiometric lithium metatitanate ($Li_2TiO_3+TiO_2$) and lithium metazirconate ($Li_2ZrO_3+ZrO_2$) pebbles, fabricated using a extrusion-spheronization-sintering process, are considered as alternative candidates for the ceramic breeder material. In order to compare the long-term behavior of the three materials at HCPB-blanket relevant temperature and atmospheric (He+0.1% $H_2$), a campaign of three long time annealing expts. were carried out at Forschungszentrum Karlsruhe (FZK). Pebbles of each ceramic breeder material ($Li_4SiO_4+SiO_2$ from FZK, $Li_2TiO_3+TiO_2$ and $Li_2ZrO_3+ZrO_2$ from CEA) were annealed for 96 days at 970 °C. During this period the change of the mech. characteristics, the microstructure, and the chemical composition of the pebbles was analyzed. After the end of the annealing experiment, uniaxial compression tests of pebble beds were performed addnl. In the present paper the results from the second exptl. campaign are reported and discussed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:415887 HCAPLUS
DOCUMENT NUMBER: 135:227218
TITLE: Syntheses of racemic and non-racemic silicon- and germanium-containing α-amino acids of the

formula type H2NCH(CH2ElR3)COOH (El=Si, Ge; R=organyl) and incorporation of D-H2NCH(CH2SiMe3)COOH and D-H2NCH(CH2GeMe3)COOH into biologically active decapeptides: a study on C/Si/Ge bioisosterism

AUTHOR(S): Merget, Marcus; Gunther, Kurt; Bernd, Michael; **Gunther, Eckhard**; Tacke, Reinhold

CORPORATE SOURCE: Institut fur Anorganische Chemie, Universitat Wurzburg, Wurzburg, D-97074, Germany

SOURCE: Journal of Organometallic Chemistry (2001), 628(2), 183-194
CODEN: JORCAI; ISSN: 0022-328X

PUBLISHER: Elsevier Science S.A.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:227218

AB Two novel efficient methods for the synthesis of racemic silicon- and germanium-containing α-amino acids of the formula type rac-H2NCH(CH2ElR3)COOH (El = Si, Ge; R = organyl ), starting from 3,6-diethoxy-2,5-dihydropyrazine, have been developed. Racemic α-amino acids synthesized: rac-H2NCH(CH2SiMe3)COOH (rac-2), rac-H2NCH(CH2GeMe3)COOH (rac-3), rac-H2NCH(CH2SiMe2Ph)COOH (rac-4), rac-H2NCH(CH2GeMe2Ph)COOH (rac-5), and rac-H2NCH(CH2SiMe2CH:CH2)COOH (rac-6). Preparative liquid-chromatog. resolution of rac-2 and rac-3 [CHIROBIOTIC T (glycopeptide Teicoplanin covalently linked to spherical silica gel) as the stationary phase] yielded the α-amino acids (R)-2, (S)-2, (R)-3, and (S)-3. The (R)- and (S)-enantiomers of β-(trimethylsilyl)alanine [(R)- and (S)-2] and β-(trimethylgermyl)alanine [(R)- and (S)-3] are sila- and germa-analogs, resp., of the antipodes of the non-proteinogenic α-amino acid β-tert-butylalanine [(S)- and (R)-H2NCH(CH2CMe3)COOH; (S)- and (R)-1]. Starting from the N-Fmoc-protected C/Si/Ge-analogous (D-configuration) α-amino acids (R)-1, (S)-2, and (S)-3, the C/Si/Ge-analogous decapeptides 7-9 [Ac-D-Nal1-4-Cl-D-Phe2-D-Pal3-Ser4-N-Me-Tyr5-D-Hci6-Nle7-Arg8-Pro9-D-Me3El-Ala10-NH2 (7, El = C; 8, El = Si; 9, El = Ge)] were prepared by sequential solid-phase synthesis. The decapeptides 7-9 were studied in vitro in a functional assay using a recombinant cell line expressing the human GnRH receptor (agonist Triptorelin). Compds. 7-9 behaved as medium-potent GnRH antagonists, the antagonistic potencies of these three C/Si/Ge analogs being very similar.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:278963 HCAPLUS

DOCUMENT NUMBER: 135:10626

TITLE: Standardisation and decay data of 177Lu and 188Re

AUTHOR(S): Schotzig, U.; Schrader, H.; Schonfeld, E.; **Gunther, E.**; Klein, R.

CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt, Braunschweig, 38116, Germany

SOURCE: Applied Radiation and Isotopes (2001), 55(1), 89-96
CODEN: ARISEF; ISSN: 0969-8043

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The activity values of 177Lu and 188Re standard sources were measured using the 4πβ-γ-coincidence method and by liquid scintillation counting. The x- and gamma-ray emission probabilities per disintegration were determined by means of photon spectrometry with calibrated Ge and Si(Li) detectors and using the pertinent activity values. The half-lives were

measured with ionization chambers, yielding T1/2(177Lu) = 6.646(5) d and T1/2(188Re) = 0.70848(9) d.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:132620 HCAPLUS
DOCUMENT NUMBER: 135:353252
TITLE: Comparative genomic aspects of rat, mouse and human MHC class I gene regions
AUTHOR(S): **Gunther, E.**; Walter, L.
CORPORATE SOURCE: Abteilung Immungenetik, Georg-August-Universitat, Gottingen, D-37073, Germany
SOURCE: Cytogenetics and Cell Genetics (2000), 91(1-4), 107-112
CODEN: CGCGBR; ISSN: 0301-0171
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. In this review a particular aspect of the genomic structure of the major histocompatibility complex (MHC), the organization of MHC class I regions, will be discussed for the rat in comparison to mouse and human.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:48557 HCAPLUS
DOCUMENT NUMBER: 134:196851
TITLE: Manufacturing and characterization of piezoceramic lead metaniobate PbNb2O6
AUTHOR(S): Ray, S.; **Gunther, E.**; Ritzhaupt-Kleissl, H.-J.
CORPORATE SOURCE: Forschungszentrum Karlsruhe GmbH, Institut fur Materialforschung III, Karlsruhe, D-76021, Germany
SOURCE: Journal of Materials Science (2000), 35(24), 6221-6224
CODEN: JMTSAS; ISSN: 0022-2461
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of single-phase lead metaniobate PbNb2O6 powders by a novel Thermal Two-Stage Process is described. Ceramic parts are produced from these powders by dry pressing and sintering. Following polarization, the piezoelec. properties of the specimens are measured. The piezoelec. material data of the specimens from this novel processing route are comparable with the values known from literature.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:894792 HCAPLUS
DOCUMENT NUMBER: 134:141823
TITLE: New LHRH antagonists with enhanced biological activity: Preclinical and clinical results
AUTHOR(S): Kutscher, Bernhard; Bernd, Michael; **Gunther, Eckhard**; Deger, Wolfgang; Reissmann, Thomas; Beckers, Thomas; Deghenghi, Romano; Engel, Jurgen
CORPORATE SOURCE: Corporate Research, ASTA Medica AG, Frankfurt, D-60314, Germany
SOURCE: Peptides for the New Millennium, Proceedings of the

American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 655-657. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A brief review/discussion with 4 refs. on the title topic with focus on Cetrorelix, Antarelix, and D-26344 and their use in treating sex hormone-dependent tumors and nonmalignant conditions.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:883024 HCAPLUS
DOCUMENT NUMBER: 134:126130
TITLE: Molecular dynamics simulations of the binding of a GnRH agonist to a model GnRH receptor
AUTHOR(S): ter Laak, A. M.; Kuhne, R.; Krause, G.; Polymeropoulos, E. E.; Kutscher, B.; **Gunther, E.**
CORPORATE SOURCE: Forschungsinstitut fur Molekulare Pharmakologie, Berlin, 10315, Germany
SOURCE: Molecular Modeling and Prediction of Bioactivity, [Proceedings of the European Symposium on Quantitative Structure-Activity Relationships: Molecular Modeling and Prediction of Bioactivity], 12th, Copenhagen, Denmark, Aug. 23-28, 1998 (2000), Meeting Date 1998, 397-398. Editor(s): Gundertofte, Klaus; Jorgensen, Flemming Steen. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69ASO3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Gonadotropin-releasing hormone (GnRH) is the naturally occurring agonist for the G-protein-coupled GnRH receptor. GnRH stimulates the pituitary gland to produce LH and FSH, and both GnRH agonists and antagonists are potentially useful in the treatment of hormone dependent ailments. The aim of the present modeling study is the generation of a 3D-model for the binding of GnRH agonists to the GnRH receptor model using a mol. dynamics protocol with carefully designed range distance restraint functions. At a second stage in the same mol. dynamics run, the possible conformational changes within the receptor after agonist binding are investigated by simulating hypothetical conformational changes of selected conserved amino acid side chains within the GnRH receptor.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:744589 HCAPLUS
DOCUMENT NUMBER: 134:49835
TITLE: Microstructure and piezoelectric properties of lead metaniobate PbNb2O6
AUTHOR(S): Ray, S.; Sauermann, Y.; Paul, F.; **Gunther, E.** ; Ritzhaupt-Kleissl, H. -J.
CORPORATE SOURCE: Forschungszentrum Karlsruhe GmbH, Institut fur Materialforschung III, Germany
SOURCE: EUROMAT 99, Biannual Meeting of the Federation of European Materials Societies (FEMS), Munich, Germany,

Sept. 27-30, 1999 (2000), Meeting Date 1999, Volume 13, 428-432. Editor(s): Grassie, K. Wiley-VCH Verlag GmbH: Weinheim, Germany.
CODEN: 69AMNI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In this contribution an overview is given of the influence of various processing parameters, sintering parameters in particular, on the development of the microstructure of piezoceramic samples made of lead metaniobate PbNb2O6. Also, the influence of the microstructure on the resulting piezoelec. properties of the material is discussed briefly.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 21 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:666761 HCAPLUS
DOCUMENT NUMBER: 133:256821
TITLE: Novel LHRH antagonists with improved solubility characteristics
INVENTOR(S): Bernd, Michael; Kutscher, Bernhard; **Gunther, Eckhard**; Romeis, Peter; Reissmann, Thomas; Beckers, Thomas
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000055190 | A1 | 20000921 | WO 2000-EP2165 | 20000311 |
| W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19911771 | A1 | 20000928 | DE 1999-19911771 | 19990317 |
| CA 2381461 | AA | 20000921 | CA 2000-2381461 | 20000311 |
| BR 2000009472 | A | 20011127 | BR 2000-9472 | 20000311 |
| EP 1163264 | A1 | 20011219 | EP 2000-910816 | 20000311 |
| EP 1163264 | B1 | 20040922 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200103339 | T2 | 20020422 | TR 2001-200103339 | 20000311 |
| JP 2002543045 | T2 | 20021217 | JP 2000-605616 | 20000311 |
| AU 759442 | B2 | 20030417 | AU 2000-32887 | 20000311 |
| NZ 514830 | A | 20030530 | NZ 2000-514830 | 20000311 |
| RU 2227145 | C2 | 20040420 | RU 2001-128232 | 20000311 |
| AT 277077 | E | 20041015 | AT 2000-910816 | 20000311 |
| PT 1163264 | T | 20041231 | PT 2000-910816 | 20000311 |
| ES 2225103 | T3 | 20050316 | ES 2000-910816 | 20000311 |
| NO 2001004486 | A | 20011102 | NO 2001-4486 | 20010914 |
| ZA 2001007753 | A | 20020513 | ZA 2001-7753 | 20010919 |
| BG 106008 | A | 20020628 | BG 2001-106008 | 20011011 |
| HK 1045531 | A1 | 20050520 | HK 2002-107028 | 20020926 |
| US 2004266695 | A1 | 20041230 | US 2003-671573 | 20030929 |
| PRIORITY APPLN. INFO.: | | | DE 1999-19911771 A | 19990317 |
| | | | WO 2000-EP2165 W | 20000311 |

US 2000-525007 A3 20000314

OTHER SOURCE(S): MARPAT 133:256821

AB The invention relates to peptides which contain N-methylated amino acid building blocks and are provided with improved water solubility Medicaments containing the inventive peptides can be used for the treatment of hormone-dependent tumors and hormone-influenced, non-malignant diseases.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:509345 HCAPLUS

DOCUMENT NUMBER: 133:157847

TITLE: Structural investigations on the oxidenitrides SrTaO2N, CaTaO2N and LaTaON2 by neutron and x-ray powder diffraction

AUTHOR(S): **Gunther, E.**; Hagenmayer, R.; Jansen, M.

CORPORATE SOURCE: Max-Planck-Inst. Festkorperforschung, Stuttgart, D-70569, Germany

SOURCE: Zeitschrift fuer Anorganische und Allgemeine Chemie (2000), 626(7), 1519-1525
CODEN: ZAACAB; ISSN: 0044-2313

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: German

AB The crystal structures of the perovskite related oxidenitrides SrTaO2N, LaTaON2, and CaTaO2N were determined with special regard to the structures of the resp. anionic partial structure. The structure refinements were performed by individual Rietveld analyses of both x-ray and neutron powder diffractograms and in addition by joint refinements to confirm the results. Both refinement methods yield consistent structure solns. At least the 1st 2 compds. have fully ordered anionic sublattices. The crystal structure of SrTaO2N was solved in the space group I4/mcm (a = 5.7049(3), c = 8.0499(5) Å, RP = 0.0706, Rwp = 0.0904, reflections: 70 (neutrons)/36 (x-ray), R(F2)(n) = 0.147, R(F2)(X) = 0.0952), with an ordered anionic partial structure. LaTaON2 crystallizes monoclinic (C2/m, a = 8.0922(3), b = 8.0603(2), c = 5.7118(2) Å, β = 134.815(1)°, Rp = 0.0592, RwP = 0.0766, reflections: 235(n)/113(X), R(F2)(n) = 0.0944, R(F2)(X) = 0.165) and also shows a totally ordered distribution of the anions. In the case of CaTaO2N (Pnma, a = 5.6239(3), b = 7.8954(4), c = 5.5473(3) Å, Rp = 0.0503, Rwp = 0.0656, reflections 206(n)/110(X), R(F2)(n) = 0.0985, R(F2)(X) = 0.0405) slightly unbalanced displacement parameters (neutron data, ordered O/N distribution model) hint at a partial exchange of O and N.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 23 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:318656 HCAPLUS

DOCUMENT NUMBER: 133:28908

TITLE: Tissue transglutaminase in the small intestine of the mouse as a marker for apoptotic cells. Colocalization with DNA fragmentation

AUTHOR(S): Aschoff, A. P.; **Gunther, E.**; Jirikowski, G. F.

CORPORATE SOURCE: Department of Anatomy II, FSU-Jena, Jena, 07743, Germany

SOURCE: Histochemistry and Cell Biology (2000), 113(4), 313-317
CODEN: HCBIFP; ISSN: 0948-6143

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Besides the morphol. changes in cells undergoing apoptosis, such as chromatin condensation and cell shrinkage, histol. demonstration of DNA fragmentation by in situ end labeling (ISEL) has been widely used for the demonstration of apoptotic cells in tissue sections. Although DNA fragmentation can be demonstrated in apoptotic cells and apoptotic bodies in most cases, there is no clear correlation of ISEL staining with apoptosis. It has often been demonstrated that, in many morphol. intact cells, nuclei with fragmented DNA can be found. Thus staining with ISEL for the detection of apoptosis is useful only in connection with other markers for apoptosis as, for example, characteristic morphol. changes. Here we show that tissue transglutaminase protein is unequivocally expressed in apoptotic enterocytes as shown by DNA fragmentation and morphol. Tissue transglutaminase is not expressed in enterocytes with healthy morphol., although DNA fragmentation can be demonstrated in these cells. Thus the immunohistochem. demonstration of tissue transglutaminase may serve as a simple marker for apoptotic epithelial cells in tissue sections.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:292155 HCAPLUS
DOCUMENT NUMBER: 133:115600
TITLE: Report on rat chromosome 20
AUTHOR(S): Butcher, G.; **Gunther, E.**; Gill, T. J., III; Kunz, H. W.; Natori, T.
CORPORATE SOURCE: Immunology Department, The Babraham Institute, Cambridge, CB2 4AT, UK
SOURCE: Journal of Experimental Animal Science (1999), 40(1-3), 143-153
CODEN: JEXSEU; ISSN: 0939-8600
PUBLISHER: Urban & Fischer Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 147 refs. compiling the 120 genes, 4 QTL, and about 125 DNA markers that have been mapped to rat chromosome 20. Several recent reports of maps are available that are based mainly on microsatellite markers.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:292142 HCAPLUS
DOCUMENT NUMBER: 133:115587
TITLE: Report on rat chromosome 7
AUTHOR(S): **Gunther, E.**; Levan, G.
CORPORATE SOURCE: Division of Immunogenetics, University of Gottingen, Gottingen, D - 37073, Germany
SOURCE: Journal of Experimental Animal Science (1999), 40(1-3), 63-68
CODEN: JEXSEU; ISSN: 0939-8600
PUBLISHER: Urban & Fischer Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 41 refs. A compilation of the genes mapped to rat chromosome 7 is provided, as well as a cytogenetic map, linkage maps, and framework markers.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 26 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:281531 HCAPLUS
DOCUMENT NUMBER: 132:304251
TITLE: Proceedings of the International Workshop on the Impact of Rat Genome Mapping on Biomedical Research, held 4-6 October 1998, in Lower Saxony, Germany. [In: J. Exp. Anim. Sci., 1999; 40(1-3)]
AUTHOR(S): **Gunther, E.**; Levan, G.; Jacob, H.; Hedrich, H. J.; Editors
CORPORATE SOURCE: Germany
SOURCE: (1999) Publisher: (Urban & Fischer: Jena, Germany), 164 pp.
DOCUMENT TYPE: Book
LANGUAGE: English
AB Unavailable

L17 ANSWER 27 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:193472 HCAPLUS
DOCUMENT NUMBER: 132:268556
TITLE: Wet chemical methods for preparation of yttrium barium copper oxide (YBCO) and bismuth strontium calcium copper oxide (BPSCCO) ceramic superconductors
AUTHOR(S): Binder, J. R.; **Gunther, E.**; Wedemeyer, H.; Ritzhaupt-Kleissl, H.-J.; Hausselt, J. H.
CORPORATE SOURCE: Forschungszentrum Karlsruhe GmbH, Institut fur Materialforschung III, Germany
SOURCE: Werkstoffwoche '98, Band VII: Symposium 9, Keramik; Symposium 14, Simulation Keramik, Munich, Sept., 1998 (1999), Meeting Date 1998, 175-180. Editor(s): Heinrich, Juergen. Wiley-VCH Verlag GmbH: Weinheim, Germany.
CODEN: 68SUAA
DOCUMENT TYPE: Conference; General Review
LANGUAGE: German
AB A review with 9 refs. is given on manufacturing high-performance functional ceramics with uniform dopant distribution, shortened total time, and reduced sintering temperature Thin-film YBa2Cu3O7-x (YBCO) superconductor on monocryst. SrTiO3 substrate can be prepared by a sol-gel method. Fine-scaled Pb-doped Bi2Sr2Ca2Cu3O10+x (BSCCO) superconductor powders can be prepared by a thermal two-stage procedure. Powders obtained thereby show excellent bulk material properties with good consolidation.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 28 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:192263 HCAPLUS
DOCUMENT NUMBER: 132:213777
TITLE: Standardization of 237Np by the CIEMAT/NIST LSC tracer method
AUTHOR(S): **Gunther, E.**
CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, 38116, Germany
SOURCE: Applied Radiation and Isotopes (2000), 52(3), 471-474
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The standardization of 237Np presents some difficulties: several groups of

alpha, beta and gamma radiation, chemical problems with the daughter nuclide 233Pa, an incomplete radioactive equilibrium after sample preparation, and high conversion of some gamma transitions. To solve the chemical problems, a sample composition involving the Ultima Gold AB scintillator and a high concentration of HCl was used. Standardization by the CIEMAT/NIST method using the 3H tracer nuclide and by pulse shape discrimination is described. The results agree within 0.1% with those obtained by two other methods.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 29 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:754855 HCAPLUS
DOCUMENT NUMBER: 134:96034
TITLE: Major histocompatibility complex-linked MIC genes in rhesus macaques and other primates
AUTHOR(S): Seo, J.-W.; Bontrop, R.; Walter, L.; **Gunther, E.**
CORPORATE SOURCE: Abteilung Immungenetik, Georg-August-Universitat Gottingen, Gottingen, D-37037, Germany
SOURCE: Immunogenetics (1999), 50(5/6), 358-362
CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A group of class I genes has been identified in the human major histocompatibility complex (MHC), the HLA complex, that exhibit an organization similar to class Ia genes, but the gene products are only about 15-35% identical compared with various domains of class Ia mols. These novel genes, designated MIC or PERB11 occur in several copies, MICA (PERB11.1) to MICE (PERB11.5). To facilitate use of animal models, we have started to examine MIC genes in nonhuman primates. Here we clone, characterize and sequence MICA/B-like genes from Macaca mulatta, Papio hamadryas and Ateles fusciceps. Our results presented here confirm and extend the recent publication of primate MIC gene sequences (Steinle et al. 1998), and contribute to the delineation of their evolution. We found that MIC genes of M. mulatta and P. hamadryas are not orthologs of either human MICA or MICB, but these MIC genes appear to be derived from the same MIC ancestor gene which duplicated and diversified in the various primate species.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 30 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:641376 HCAPLUS
DOCUMENT NUMBER: 132:10068
TITLE: M protein of a Streptococcus dysgalactiae human wound isolate shows multiple binding to different plasma proteins and shares epitopes with keratin and human cartilage
AUTHOR(S): Geyer, A.; Roth, A.; Vettermann, S.; **Gunther, E.**; Groh, A.; Straube, E.; Schmidt, K.-H.
CORPORATE SOURCE: Institute of Medical Microbiology, Hospital of the Friedrich-Schiller-University, Jena, D-07740, Germany
SOURCE: FEMS Immunology and Medical Microbiology (1999), 26(1), 11-24
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Besides group A (GAS), Lancefield group C β-hemolytic streptococci (GCS) have been implicated as a causative agent in outbreaks of purulent pharyngitis. In this study we have investigated a class CI M protein of a Streptococcus dysgalactiae human wound isolate designated MC. MC shares similar properties with M proteins of GAS. It contributes to the virulence of the investigated GCS strain as revealed by in vivo phagocytosis in chicken embryos. Further, MC showed multiple binding to the human plasma proteins fibrinogen, albumin, plasminogen, IgA and all subclasses of IgG. Until now, an M protein, especially from a group C strain, with such a multiple binding behavior has not been described. Immunoblot expts. with 150 patient sera, having a rheumatoid factor titer > 1:256, revealed that 26% of these sera showed serol. cross-reactivity between a 68-kDa cartilage protein and the N-terminal part of MC. Only 8% of the sera of healthy patients showed this property. In addition, MC also cross-reacted with antibodies recognizing epidermal keratins. The cross-reacting 68-kDa protein from cartilage was different from human serum albumin, but was recognized with anti-vimentin immune serum. The MC was cloned and the gene sequenced. By using PCR, recombinant gene fragments encoding characteristic peptide fragments of MC were expressed in Escherichia coli. The peptides were used to map the binding sites for plasma proteins and to locate the cross-reacting epitopes on the MC mol. In consequence, sequence alignments revealed that MC shared homologous regions with vimentin and different keratins. Our data, obtained with MC, suggest that not only infections with GAS but also infections with GCS and possibly GGS (the latter species can also produce class CI M-like proteins) may be responsible for the formation of streptococcal-associated sequel diseases.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 31 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:572216 HCAPLUS

DOCUMENT NUMBER: 131:272102

TITLE: A practical synthesis of benzyl α- and allyl β-D-glucopyranosides regioselectively substituted with (CH2)3OH groups. Stereocontrolled β-galactosidation by cation π-interaction

AUTHOR(S): Neda, Ion; Sakhaii, Peyman; Wassmann, Anke; Niemeyer, Ulf; **Gunther, Eckhard**; Engel, Jurgen

CORPORATE SOURCE: Institut Anorganische Analytische Chemie, Technische Univ. Braunschweig, Braunschweig, D-38023, Germany

SOURCE: Synthesis (1999), (9), 1625-1632
CODEN: SYNTBF; ISSN: 0039-7881

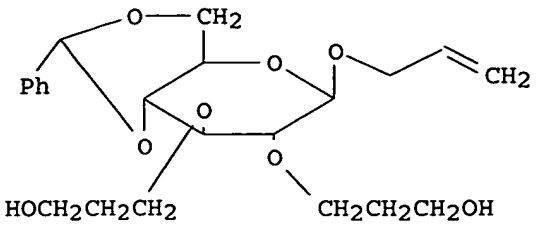
PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal

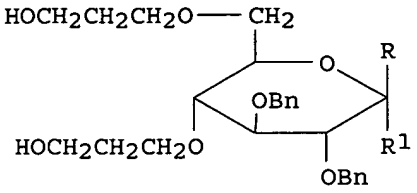
LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:272102

GI




I




II

AB Efficient synthesis of the 2,3- or 4,6-di-O-hydroxypropyl-functionalized glucose derivs. I and II (R = allyloxy, R1 = H; R = H, R1 = PhCH2O) is presented. These compds. represent potential precursors for the synthesis of multi-antennary oligosaccharides. A new method was developed for the β-stereoselective galactosylation using galactosyl difluorophosphate as galactosyl donor and tetra-O-propylated cone-calix[4]arene as stabilizer for the oxo-carbenium ion. The latter compound is intended to serve (via immobilization on solid phase and subsequent deprotection) as affinity ligand in the isolation of tumor cell lectins via affinity chromatog.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 32 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:470418 HCAPLUS
DOCUMENT NUMBER: 131:232261
TITLE: Production of piezoceramic powders by the thermal two-stage process
AUTHOR(S): Weddigen, A.; Hennige, V. D.; **Gunther, E.**; Ritzhaupt-Kleissl, H.-J.
CORPORATE SOURCE: Forschungszentrum Karlsruhe, Institut fur Material forschung III, Karlsruhe, 76021, Germany
SOURCE: Journal of Materials Science (1999), 34(14), 3461-3465
CODEN: JMTSAS; ISSN: 0022-2461
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present paper describes the production of lead zirconate titanate (PZT) with different additives and of lead metaniobate (PN) by means of the Thermal Two-Stage Process. This process, especially developed for the synthesis of multicomponent ceramic powders is characterized by the following: the starting constituents are liquid metalorg. precursors, such as alcoholates or acetates, which are converted to a homogeneous, multicomponent ceramic powder by spray drying the liquid precursors, resulting in an organic granulate, which is then followed by the thermal conversion of this organic

powder into the final ceramic material. The resulting ceramic powder shows favorable properties with respect to homogeneity and further processing, e.g. pressing and sintering of compacts. The efficiency of the process will be demonstrated by the characterization of the piezoelec. properties of the sintered compacts.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 33 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:362795 HCAPLUS
DOCUMENT NUMBER: 131:180515
TITLE: Sequence analysis of the genomic interval between the Rps18 and RT1-A genes in the RT1u haplotype
AUTHOR(S): Walter, L.; **Gunther, E.**
CORPORATE SOURCE: Division of Immunogenetics, University of Gottingen, Gottingen, 37073, Germany
SOURCE: Transplantation Proceedings (1999), 31(3), 1513-1514
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors sequence and map the genomic interval between the rat genes Rps18 and RT1-A of the MHC RT1u haplotype.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 34 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:349427 HCAPLUS
DOCUMENT NUMBER: 131:64146
TITLE: Standardization and decay data of 153Sm
AUTHOR(S): Schotzig, U.; Schonfeld, E.; **Gunther, E.**; Klein, R.; Schrader, H.
CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, D-38116, Germany
SOURCE: Applied Radiation and Isotopes (1999), 51(2), 169-175
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The activity concentration of a 153Sm solution was determined by $4\pi\beta$-$\gamma$ coincidence measurements and by liquid scintillation counting (LSC). Both methods yielded results which differ by only 0.1%, the relative standard uncertainty being 0.1 and 0.2%, resp. X-ray and gamma-ray emission probabilities of several transitions were measured; they were used to calculate beta transition probabilities. The emission probabilities of the 69.7 and the 103.2 keV gamma rays were found to be 0.0465 $\pm$ 0.0005 and 0.2923 $\pm$ 0.0018, resp.; and the half-life was found to be (46.274$\pm$0.007) h.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 35 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:244571 HCAPLUS
DOCUMENT NUMBER: 130:276778
TITLE: Methods of modulating serine/threonine protein kinase function with 5-azaquinoxaline-based compounds, compound preparation, and therapeutic use
INVENTOR(S): McMahon, Gerald; Kutscher, Bernhard; **Gunther, Eckhard**; App, Harald
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany

SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9917759 | A2 | 19990415 | WO 1998-US20910 | 19981005 |
| WO 9917759 | A3 | 20000106 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9808961 | A | 19991004 | ZA 1998-8961 | 19981001 |
| CA 2306257 | AA | 19990415 | CA 1998-2306257 | 19981005 |
| AU 9895141 | A1 | 19990427 | AU 1998-95141 | 19981005 |
| AU 757585 | B2 | 20030227 | | |
| EP 1028729 | A2 | 20000823 | EP 1998-948606 | 19981005 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO | | | | |
| BR 9814814 | A | 20001003 | BR 1998-14814 | 19981005 |
| TR 200000906 | T2 | 20001121 | TR 2000-200000906 | 19981005 |
| US 6180631 | B1 | 20010130 | US 1998-166723 | 19981005 |
| JP 2001518496 | T2 | 20011016 | JP 2000-514630 | 19981005 |
| TR 200100385 | T2 | 20020621 | TR 2001-200100385 | 19981005 |
| NZ 503431 | A | 20020726 | NZ 1998-503431 | 19981005 |
| RU 2223753 | C2 | 20040220 | RU 2000-111434 | 19981005 |
| MX 200003255 | A | 20001110 | MX 2000-3255 | 20000403 |
| NO 2000001748 | A | 20000405 | NO 2000-1748 | 20000405 |
| BG 104392 | A | 20001229 | BG 2000-104392 | 20000428 |
| US 6727252 | B1 | 20040427 | US 2000-688199 | 20001016 |
| HK 1031836 | A1 | 20050401 | HK 2001-102529 | 20010410 |
| PRIORITY APPLN. INFO.: | | | US 1997-61123P P | 19971006 |
| | | | US 1998-166723 A3 | 19981005 |
| | | | WO 1998-US20910 W | 19981005 |

OTHER SOURCE(S): MARPAT 130:276778

AB Methods are provided for modulating the function of serine/threonine protein kinases with 5-azaquinoxaline-based compds. The methods incorporate cells that express a serine/threonine protein kinase, e.g. RAF. In addition,methods are described for preventing and treating serine/threonine protein kinase-related abnormal conditions (e.g. cancer) in organisms with a compound identified by the invention. Furthermore, the invention pertains to 5-azaquinoxaline compds., their preparation, and pharmaceutical compns. comprising them.

L17 ANSWER 36 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:64168 HCAPLUS
DOCUMENT NUMBER: 130:279968
TITLE: Heterogeneous patterns of constitutive and heat shock induced expression of HLA-linked HSP70-1 and HSP70-2 heat shock genes in human melanoma cell lines
AUTHOR(S): Dressel, R.; Johnson, J. P.; **Gunther, E.**
CORPORATE SOURCE: Division of Immunogenetics, University of Gottingen, Gottingen, D-37073, Germany

SOURCE: Melanoma Research (1998), 8(6), 482-492
CODEN: MREEEH; ISSN: 0960-8931
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The heat shock response, which is characterized by the induction of heat shock proteins, is known to affect the ability of tumor cells to cope with potentially adverse conditions such as hypoxia, glucose starvation and cytotoxic immune reactions. To assess the heat shock response of melanoma cells, spontaneous and heat shock induced expression of heat shock proteins was analyzed in a panel of 17 human melanoma cell lines. Constitutive expression of HSP27, HSP70, HSC70, HSP90αβ and GRP94 proteins was found in all the melanoma cell lines, and HSP70 and HSC70 were also induced by heat shock. The major heat inducible HLA-linked HSP70-1 and HSP70-2 genes were analyzed at the mRNA level. Basal expression and inducibility varied between the different melanoma cell lines. In addition, in situ hybridization demonstrated heterogeneous expression of these genes among single cells of a given cell line. In general, each melanoma cell line appears to exhibit an individual type of HSP70 expression that might reflect selection during tumor progression and therapy.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 37 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:771850 HCAPLUS
DOCUMENT NUMBER: 130:164920
TITLE: Intercomparisons 1996 - 1998: Uranium, 210Pb, 3H, 14C and thorium in urine
AUTHOR(S): **Gunther, E.**; Hartmann, M.; Naurmann, M.
CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt, Braunschweig, Germany
SOURCE: Fortschritte im Strahlenschutz (1998), FS-98-98-T(Nichtionisierende Strahlung mit ihr Leben in Arbeit und Umwelt, Band I), 352-357
CODEN: FSTRER; ISSN: 1013-4506
PUBLISHER: Verlag TUV Rheinland GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with 10 refs. The working group "Incorporation Monitoring (AKI)" of the German-Swiss Radiation protection Association (FS) has performed interlab. comparisons of radionuclides in urine for many years. Since 1997, the intercomparisons have been carried out by the Bundesamt fur Strahlenschutz (BfS) in collaboration with the Physikalisch-Technische Bundesanstalt (PTB). The results of intercomparisons of uranium, lead-210 (both in 1996), tritium (1997), thorium (1998) und carbon-14 (1998) in urine will be presented here.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 38 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:483041 HCAPLUS
DOCUMENT NUMBER: 129:183548
TITLE: International comparison of measurements of the specific activity of tritiated water
AUTHOR(S): Makepeace, J.; Altzitzoglou, T.; Cassette, P.; Dryak, P.; **Gunther, E.**; Verrezen, F.; Broda, R.; Simpson, B.; Unterweger, M.
CORPORATE SOURCE: NPL, Teddington, TW11 0LW, UK
SOURCE: Applied Radiation and Isotopes (1998), 49(9-11),

1411-1416
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An international comparison of measurements of the specific activity of tritiated H2O was carried out under the auspices of the ICRM Radionuclide Techniques Working Group. The comparison, in which nine labs. participated, involved the measurement of tritiated H2O samples of unknown specific activity at up to three different activity levels. The results of the comparison are reported, together with information on the measurement techniques employed and the measurement uncertainties.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 39 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:483040 HCAPLUS
DOCUMENT NUMBER: 129:183547
TITLE: Comparison of activity concentration measurement of 63Ni and 55Fe in the framework of the EUROMET 297 project
AUTHOR(S): Cassette, P.; Altzitzoglou, T.; Broda, R.; Colle, R.; Dryak, P.; De Felice, P.; **Gunther, E.**; Arcos, J. M. Los; Ratel, G.; Simpson, B.; Verrezen, F.
CORPORATE SOURCE: BNM-LPRI, CEA/DAMRI, Gif-sur-yvette, 91193, Fr.
SOURCE: Applied Radiation and Isotopes (1998), 49(9-11), 1403-1410
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eleven labs. participated in an intercomparison of activity concentration measurements using liquid scintillation counting (LSC) for the standardization of 63Ni and 55Fe in the frame of the EUROMET project Number 297 and under the coordination of LPRI. The purpose of this action was to compare the main LSC activity concentration measurement methods currently used in radioactive metrol., and to exchange models and ideas on LSC. This paper presents a summary of the results reported by the participant labs. and an overview of the measurement methods used.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 40 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:482976 HCAPLUS
DOCUMENT NUMBER: 129:183534
TITLE: Standardization of the EC nuclides 55Fe and 65Zn with the CIEMAT/NIST LSC tracer method
AUTHOR(S): **Gunther, E.**
CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, 38116, Germany
SOURCE: Applied Radiation and Isotopes (1998), 49(9-11), 1055-1060
CODEN: ARISEF; ISSN: 0969-8043
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study is made of the standardization of 55Fe and 65Zn under different exptl. and theor. conditions. Sample composition, tracer nuclide, ionization quench approxns., kB values and approxns. for the average L Auger electron

energy, were varied to find out the optimum conditions. A standardization of 55Fe and 65Zn is possible with a relative standard uncertainty of .apprx.0.5% using 54Mn as a tracer. However, the expts. with 3H as a tracer show that the EC. decay model and the LSC theory which are included in the CIEMAT/NIST programs are not fully satisfactory for these two EC radionuclides.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 41 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:64556 HCAPLUS
DOCUMENT NUMBER: 128:131356
TITLE: Development of ceramic micro heat exchanger
AUTHOR(S): Knitter, R.; **Gunther, E.**
CORPORATE SOURCE: institut fur Materialforschung III, Forschungszentrum Karlsruhe GmbH, Karlsruhe, D-76201, Germany
SOURCE: Neue Werkstoffkonzepte, Symposium 9, Werkstoffwoche '96, Stuttgart, 1996 (1997), Meeting Date 1996, 221-226. Editor(s): Schmidt, H.; Singer, R. F. DGM Informationsgesellschaft: Oberursel, Germany. CODEN: 65OAAB
DOCUMENT TYPE: Conference
LANGUAGE: German
AB Two processes: (i) foil casting and stamping and (ii) slip casting on pyrolyzed filaments for the manufacture of the title heat exchanger are described, and the features of the heat exchangers prepared by these 2 processes are compared.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 42 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:3638 HCAPLUS
DOCUMENT NUMBER: 128:125147
TITLE: Studies on streptococcal NAD-glycohydrolase: copurification of streptodornase A
AUTHOR(S): Gerlach, D.; Ozegowski, J. H.; **Gunther, E.**; Vettermann, S.; Kohler, W.
CORPORATE SOURCE: Inst. Experimentelle Mikrobiol., Friedrich-Schiller-Universitaet Jena, Jena, D-07745, Germany
SOURCE: Advances in Experimental Medicine and Biology (1997), 418(Streptococci and the Host), 601-603 CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method for the rapid isolation of NAD glycohydrolase is described. The method gave a yield of .apprx.30% with a 968-flod purification In addition, a method for the first purification of streptodornase A, one of the 4 known streptococcal DNases, is described.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 43 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:59394 HCAPLUS
DOCUMENT NUMBER: 122:99055
TITLE: Purification and characterization of streptolysin O secreted by Streptococcus equisimilis (group C)
AUTHOR(S): Gerlach, D.; Koehler, W.; **Gunther, E.**; Mann, K.
CORPORATE SOURCE: Institute of Experimental Microbiology, Jena, D-07745,

Germany
SOURCE: Zentralblatt fuer Bakteriologie, Supplement (1994), 24(Bacterial Protein Toxins), 341-2
CODEN: ZBASE2; ISSN: 0941-018X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Streptolysin O (SLO) was purified from culture supernatants of group C streptococci. The final product was either the complete mol. (SLOn, isoelec. point 6.0) with the N-terminal sequence (Asp)-Ser-Asn-Lys-Gln-Asn-Thr-Ala-Asn-Thr-Glu-Thr- or a large fragment (SLOf, isoelec. point 7.3) with the N-terminal sequence Ala-Pro-Lys-Glu-Met-Pro-Leu-Glu-Ser-Ala-Glu-Lys-Glu-Glu-Lys- corresponding to residues 79 to 93 of a DNA-derived sequence.

L17 ANSWER 44 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:639591 HCAPLUS
DOCUMENT NUMBER: 121:239591
TITLE: Standardization and decay data of 68Ge/68Ga
AUTHOR(S): Schonfeld, E.; Schotzig, U.; **Gunther, E.**; Schrader, H.
CORPORATE SOURCE: Physikalisch-Technische Bundesanstalt, Bundesallee, D-38116, Germany
SOURCE: Applied Radiation and Isotopes (1994), 45(9), 955-61
CODEN: ARISEF; ISSN: 0883-2889
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gamma and an x-ray spectrometer, $4\pi\beta$-$\gamma$-coincidence equipment, liquid-scintillation counting (LSC) equipment and a calibrated ionization chamber (IC) have been used to determine the decay scheme parameters of 68Ga and the specific activity of a 68Ge/68Ga solution The transition probability of the positron branch and the EC branch to the ground state of 68Zn, b1 and e1, the corresponding branches to the 1077 keV level of 68Zn, b2 and e2, the total emission probability of annihilation radiation from the 68Ga decay, pann, and the gamma-ray emission probabilities of the quanta corresponding to the 1077 keV transition (p1077) and to some weak transitions were redetd. The results are b1 = 0.8785 ± 0.0012, e1 = 0.0892 ± 0.0012, b2 = 0.0129 ± 0.004, e2 = 0.0193 ± 0.0004, pann = 1.7829 ± 0.0022, p1077 = 0.0322 ± 0.0003. The specific activity of a 68Ge/68Ga solution was determined with a relative uncertainty of 1% ($1\sigma$) using $4\pi\beta$-$\gamma$ coincidence, LSC and IC measurements. A half-life of T12 = (270.99 ± 0.19) d for 68Ge was obtained by measurements with an ionization chamber.

L17 ANSWER 45 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:467389 HCAPLUS
DOCUMENT NUMBER: 97:67389
TITLE: Immune complex type disease induced by mercury(II) chloride in Brown-Norway rats: genetic control of susceptibility
AUTHOR(S): Sapin, Catherine; Mandet, Chantal; Druet, Elvira; **Gunther, E.**; Druet, P.
CORPORATE SOURCE: Hop. Broussais, Paris, 75674/14, Fr.
SOURCE: Clinical and Experimental Immunology (1982), 48(3), 700-4
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
AB $HgCl_2$ induces a biphasic autoimmune glomerulonephritis in Brown-Norway (BN) rats, but not in Lewis (LEW) rats. The genetic control of susceptibility to both phases was investigated by testing the response of

segregants between BN and LEW rats and congenic LEW.1N rats. The susceptibility to the 1st phase, characterized by the appearance of antiglomerular basement membrane antibodies, depends on several genes 1 of which is RT1 linked. Susceptibility to the 2nd phase, which is an immune complex type glomerulonephritis, depended on 1 major RT1-linked gene or cluster of genes with a role for other(s) non-RT1 linked gene(s) controlling the magnitude of the response. However, congenic LEW.1N rats were resistant. Thus, the disease gene was lost during the strain derivation. The question of whether both phases are 2 different diseases or expression of the same process cannot be definitely answered; data however indicate a dissociation of disease processes.

L17 ANSWER 46 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1958:117472 HCAPLUS
DOCUMENT NUMBER: 52:117472
ORIGINAL REFERENCE NO.: 52:20822h-i
TITLE: The trace elements as integral constituents of ferments and their importance in agriculture
AUTHOR(S): **Gunther, E.**
SOURCE: Deut. Landwirtschaft (1956), 7, 332-7
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The influence of B, Co, Ni, Zn, Cu, Mn, Al, Mo, and Fe on the health of plants is discussed. Ranges in p.p.m. of these elements contained in various plants and soils are given. 32 references.

L17 ANSWER 47 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1956:87249 HCAPLUS
DOCUMENT NUMBER: 50:87249
ORIGINAL REFERENCE NO.: 50:16405d-e
TITLE: Stereoisomerism and excited states of simple polymethine dyes
AUTHOR(S): Baumgartner, F.; **Gunther, E.**; Scheibe, G.
CORPORATE SOURCE: Tech. Hochschule, Munich, Germany
SOURCE: Zeitschrift fuer Elektrochemie und Angewandte Physikalische Chemie (1956), 60, 570-2
CODEN: ZEAPAA; ISSN: 0372-8323
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB 1,5-N,N'-dipyrrolidylpentamethine perchlorate (I) is converted by irradiation with light of wave length 424 mμ (the principal absorption band of I) at -144° into a compound (II) with principal absorption band at 454 mμ. II reverts to I spontaneously at higher temps. with an activation energy of 5.7 kcal. I and II show fluorescence bands at 440 and 470 mμ, resp.

L17 ANSWER 48 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:46417 HCAPLUS
DOCUMENT NUMBER: 46:46417
ORIGINAL REFERENCE NO.: 46:7713e
TITLE: Vitamin C content of Germany's main medicinal and spice plants
AUTHOR(S): **Gunther, E.**; Heeger, E. F.; Rosenthal, Christine
SOURCE: Pharmazie (1952), 7, 24-50
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The vitamin C content of various samples of different parts of 81 varieties of plants was determined at different times.

L17 ANSWER 49 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1950:36771 HCAPLUS
DOCUMENT NUMBER: 44:36771
ORIGINAL REFERENCE NO.: 44:7026h-i,7027a
TITLE: Determination of the ascorbic acid oxidation power [oxidase] in plants and animal organs and tissues
AUTHOR(S): **Gunther, E.**
SOURCE: Pharmazie (1948), 3, 158-61
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The ascorbic acid content and the oxidase activity have been measured under various conditions in different parts of a variety of plants. There is no relation between the 2 quantities. The oxidase activity is greatly retarded by frost, completely inhibited at -20°, and destroyed by heating to 100°. Oxidase activity increases and ascorbic acid content decreases as the plants wither. The results do not support Wachholder's exchange theory.

L17 ANSWER 50 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1948:42772 HCAPLUS
DOCUMENT NUMBER: 42:42772
ORIGINAL REFERENCE NO.: 42:8983h-i
TITLE: The supplying of the population with natural sources of vitamin C
AUTHOR(S): Schwarze, W. K.; **Gunther, E.**
CORPORATE SOURCE: Anst. Vitaminforschung u. Vitaminprufung, Leipzig, Germany
SOURCE: Pharmazie (1946), 1, 320-2
From: Chem. Zentr. I, 534-5(1947).
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The vitamin C content of blackberry, raspberry, strawberry, birch, elderberry, walnut, violet, linden, poplar, dog-rose, and privet leaves, of linden blossoms, of mixts. of grasses, and of hip varies with the season. It is almost completely lost by simple drying or salting down of the fresh plant parts. Blanching of the coarsely cut fresh plants with steam (to destroy the enzymes) and subsequent drying in vacuum or in an ordinary drying oven at 60-90° is recommended.

L17 ANSWER 51 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1948:42771 HCAPLUS
DOCUMENT NUMBER: 42:42771
ORIGINAL REFERENCE NO.: 42:8983h-i
TITLE: The supplying of the population with natural sources of vitamin C
AUTHOR(S): Schwarze, W. K.; **Gunther, E.**
CORPORATE SOURCE: Anst. Vitaminforschung u. Vitaminprufung, Leipzig, Germany
SOURCE: Pharmazie (1946), 1, 320-2
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The vitamin C content of blackberry, raspberry, strawberry, birch, elderberry, walnut, violet, linden, poplar, dog-rose, and privet leaves, of linden blossoms, of mixts. of grasses, and of hip varies with the season. It is almost completely lost by simple drying or salting down of the fresh plant parts. Blanching of the coarsely cut fresh plants with

steam (to destroy the enzymes) and subsequent drying in vacuum or in an ordinary drying oven at 60-90° is recommended.

L17 ANSWER 52 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1947:29416 HCAPLUS
DOCUMENT NUMBER: 41:29416
ORIGINAL REFERENCE NO.: 41:5915d-f
TITLE: The determination of L-ascorbic acid by chemical methods
AUTHOR(S): Schwarze, W. K.; **Gunther, E.**
CORPORATE SOURCE: Lab. for Vitamin Research and Vitamin Testing for the Soviet Zone of Occupation, Leipzig
SOURCE: Pharmazie (1946), 1, 153-7
From: Chem. Zentr. 1947, I, 79.
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB It is shown that the wide variation of results in the determination of vitamin C by titration with 2,6-dichlorophenolindophenol is due less to the method used than to the preliminary treatment of the sample and the preparation of the extract The reducing substances other than the ascorbic acid should be determined and this value taken into consideration in the calcn. Expts. reported show that in the determination of the "blank" the ascorbic acid is destroyed by Cu salts if some HCl is added to the metaphosphate solution Moreover, the combined ascorbic acid is hydrolyzed so that the total vitamin C is determined

L17 ANSWER 53 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1941:35801 HCAPLUS
DOCUMENT NUMBER: 35:35801
ORIGINAL REFERENCE NO.: 35:5605g
TITLE: Solution of ground water problems by means of flow in thin layers
AUTHOR(S): **Gunther, E.**
SOURCE: Wasser und Abwasser (Leipzig) (1940), 38, 66
CODEN: WAABA9
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Elec. and sand models are used to determination the flow of ground water.

L17 ANSWER 54 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1941:35800 HCAPLUS
DOCUMENT NUMBER: 35:35800
ORIGINAL REFERENCE NO.: 35:5605g
TITLE: Solution of ground water problems by means of flow in thin layers
AUTHOR(S): **Gunther, E.**
SOURCE: Wasserkraft u. Wasserwirt. (1940) 49-55
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Elec. and sand models are used to determination the flow of ground water.

L17 ANSWER 55 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1937:61433 HCAPLUS
DOCUMENT NUMBER: 31:61433
ORIGINAL REFERENCE NO.: 31:8469f-g
TITLE: Rolling and sticking of sheet
AUTHOR(S): **Gunther, E.**

SOURCE: Stahl und Eisen (1937), 57, 601-4
CODEN: STEIA3; ISSN: 0340-4803
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB P, Si and to some extent C cause less sticking. High-Si transformer sheet, higher-C sheet, and alloy sheet stick so little that the rolling temperature and pressure must actually be increased to give some sticking so as to get proper rolling. Thinner sheet sticks more. Keeping the rolling pressure more uniform will make the sheet more easily separated

L17 ANSWER 56 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1934:1184 HCAPLUS
DOCUMENT NUMBER: 28:1184
ORIGINAL REFERENCE NO.: 28:184e-f
TITLE: Emulsin. XII. 1. The cleavage of phenol-β-d-isorhamnoside by emulsin
AUTHOR(S): Helferich, B.; Rohr, H.; **Gunther, E.**
SOURCE: Z. physiol. Chem. (1933), 221, 90-2
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 27, 2959. Phenol-β-d-isorhamnoside, m. 161-2°, [α]D21 -80.8°, was obtained by hydrolysis of the tri-Ac derivative, m. 134-5°, [α]D21 in CHCl3 -7.3°, prepared by Zn reduction of triacetyl-phenol-β-d-glucoside-6-bromohydrin. It is hydrolyzed by almond emulsin about twice as rapidly as the corresponding glucoside. The activity of this enzyme is strictly parallel for the 2 substrates, in different stages of enzyme purification and damage by heat or ultra-violet rays. There is no occasion to assume the existence of a specific isorhamnosidase.

L17 ANSWER 57 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1933:33542 HCAPLUS
DOCUMENT NUMBER: 27:33542
ORIGINAL REFERENCE NO.: 27:3021f-g
TITLE: Adaptation of the seedling method to the examination of moor soils
AUTHOR(S): Brune, F.; Arnd, T.; **Gunther, E.**; Poock, A.
SOURCE: Zeitschrift fuer Pflanzenernaehrung, Duengung, Bodenkunde (1932), 26A, 271-83
CODEN: ZPDBAQ; ISSN: 0372-9702
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The use of fresh soil samples, measured by volume, is recommended. If necessary, CaCO3 is added to give an equivalent of 4000 kg. of CaO per hectare. After the growth of the barley plants, roots are cut off immediately beneath the seed and analyses made of the upper portion only.

L17 ANSWER 58 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1932:39234 HCAPLUS
DOCUMENT NUMBER: 26:39234
ORIGINAL REFERENCE NO.: 26:4070c-g
TITLE: Emulsin. VII
AUTHOR(S): Helferich, B.; Winkler, S.; Gootz, R.; Peters, O.; **Gunther, E.**
SOURCE: Z. physiol. Chem. (1932), 208, 91-100
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 26, 3268. Emulsin solns. obtained by extracting the powdered press cake
of sweet almonds with dilute ZnSO4, precipitating with tannin, extracting the precipitate with

Me2CO and dissolving the residue in H2O, may be purified tenfold by treatment with Ag2O. The solution is first treated with a small quantity of Ag2O, then filtered and the residue discarded. A larger quantity of Ag2O is added to the filtrate, and the resulting precipitate decomposed by H2S. The final filtrate contains the enzyme. Several repetitions of this process yield a product with great y increased activity per unit weight of dry substance. Six phenol glucosides were used as substrates, viz., the β-d-galactoside (I), α-d-galactoside (II), α-l-arabinoside (III), β-l-arabinoside (IV), β-d-xyloside (V) and β-d-glucoside-6-bromohydrin (VI). The Ag2O treatment greatly increased the enzymic activity toward I, III, V, VI and salicin, but greatly diminished the activity toward II and IV. Similarities in the configuration of I, III, V and VI are pointed out which support the assumption that all are hydrolyzed by one and the same enzyme. The following alterations in the structure of a β-glucoside do not interfere with the activity of β-glucosidase: The 6-hydroxyl may be replaced by Br (VI), the terminal CH2OH may be replaced by H (V), the configuration at the 4-C may be reversed from d to l (I), and here again the terminal CH2OH replaced by H (III). The enzyme is therefore not sensitive to alterations in the substrate at the 4- or the 6-C atom. All 4 substrates have the same configuration at the 1-C. If this configuration is altered (II and IV), the cleavage by the purified enzyme is so small as to represent quite a different order of magnitude. A new derivative described is phenol-α-l-arabinoside (III), m. 153-5°, [α]D17 6.0°, obtained by NaOMe hydrolysis of the triacetate, m. 87-9°, [α]D19 24.7°, which in turn was prepared by condensation of PhOH in quinoline with acetobromoarabinose and Ag2O.

L17 ANSWER 59 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1932:12351 HCAPLUS
DOCUMENT NUMBER: 26:12351
ORIGINAL REFERENCE NO.: 26:1359h-i
TITLE: Can the freshness of forages be determined from their free fatty acid content?
AUTHOR(S): **Gunther, E.**
SOURCE: Chimie et Industrie (Paris) (1931), 26, 1187
CODEN: CHIEAN; ISSN: 0009-4358
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The estimation of the freshness of forage or feeds by determination of the free fatty acids gives satisfactory results with the press cakes of oil-bearing plants, but is not suitable for meat and fish meals and brans. Considerable data are given on the permissible limits of free fatty acids, fat contents, degree of rancidity and development of molds in a number of vegetable press cakes. In animal products, addition of NaCl retards the decomposition of the glycerides and prevents mold formation. Another important indication regarding the state of preservation of feeds is the presence of living mites, which require a certain amount of moisture to live.

L17 ANSWER 60 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1932:12350 HCAPLUS
DOCUMENT NUMBER: 26:12350
ORIGINAL REFERENCE NO.: 26:1359h-i
TITLE: Can the freshness of forages be determined from their free fatty acid content?
AUTHOR(S): **Gunther, E.**
SOURCE: Fortschritte der Landwirtschaft (1931), 6, 243-6
CODEN: FLWSAQ; ISSN: 0367-2557
DOCUMENT TYPE: Journal

LANGUAGE: Unavailable
AB The estimation of the freshness of forage or feeds by determination of the free fatty
acids gives satisfactory results with the press cakes of oil-bearing plants, but is not suitable for meat and fish meals and brans. Considerable data are given on the permissible limits of free fatty acids, fat contents, degree of rancidity and development of molds in a number of vegetable press cakes. In animal products, addition of NaCl retards the decomposition of the glycerides and prevents mold formation. Another important indication regarding the state of preservation of feeds is the presence of living mites, which require a certain amount of moisture to live.

L17 ANSWER 61 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1932:6694 HCAPLUS
DOCUMENT NUMBER: 26:6694
ORIGINAL REFERENCE NO.: 26:792e-f
TITLE: Action of frost on various arable soils and the resulting effect on the growth of oats and barley
AUTHOR(S): **Gunther, E.**
SOURCE: Landwirtschaftliche Jahrbuecher (1931), 73, 893-922
CODEN: LWSJAK; ISSN: 0368-8194
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB G. describes apparatus developed to study the effect of freezing. Pore space, hygroscopicity and water capacity are studied. Freezing affects all these in acid soil but has no effect on soil containing chalk. The water content is an important factor in frost action. Freezing had no effect on adsorption of soils. Freezing improved the intake of K and P of these plants which G. assumes is due to improvement in phys. condition.

L17 ANSWER 62 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1931:12330 HCAPLUS
DOCUMENT NUMBER: 25:12330
ORIGINAL REFERENCE NO.: 25:1350c
TITLE: Waste-gas utilization from the muffle furnace
AUTHOR(S): **Gunther, E.**
SOURCE: Sprechsaal (1930), 63, 975
CODEN: SPREAS; ISSN: 0341-0676
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Unavailable

L17 ANSWER 63 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1928:20739 HCAPLUS
DOCUMENT NUMBER: 22:20739
ORIGINAL REFERENCE NO.: 22:2431g-h
TITLE: The examination of the Mitscherlich procedure for the determination of the fertilizer requirements of soils
AUTHOR(S): Gerlach, M.; **Gunther, E.**; Seidel, C.
SOURCE: Zeitschrift fuer Pflanzenernaehrung, Duengung, Bodenkunde (1928), 11A, 1-29
CODEN: ZPDBAQ; ISSN: 0372-9702
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 22, 1008. The expts. carried out by the authors show that Mitscherlich cannot satisfactorily use the value of the growth factor constant and consequently the law founded on it. In the Mitscherlich equation, the total quantities of the nutrient materials used in the test must not be used, but only the part of the nutrients absorbed by the plant. The value of the growth factor constant is not constant The percent

increase in yield in two expts. is only equal when, besides the material tested, other growth factors such as the basic fertilization and the water are applied in the same amts. Therefore, the use of the Mitscherlich yield tables is not generally applicable. The Mitscherlich procedure for the determination of the fertilizer requirements of the soil gives no more than a well-conducted vegetation experiment would give.

L17 ANSWER 64 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1928:13971 HCAPLUS
DOCUMENT NUMBER: 22:13971
ORIGINAL REFERENCE NO.: 22:1644h-i
TITLE: Investigations on the Neubauer seedling method
AUTHOR(S): **Gunther, E.**
SOURCE: Zeitschrift fuer Pflanzenernaehrung, Duengung, Bodenkunde (1927), 6B, 502-6
CODEN: ZPDBAQ; ISSN: 0372-9702
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 21, 2348. Even with uniform seed, errors are associated with the method. After harvest of the seedlings, soil-sand mixture must be elutriated to determine the total mass of roots; and this introduces sources of error. Expts. showed that seedlings far from assimilated all the root-soluble nutrients in the soil.

L17 ANSWER 65 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1927:19043 HCAPLUS
DOCUMENT NUMBER: 21:19043
ORIGINAL REFERENCE NO.: 21:2348a-b
TITLE: Neubauer's "seedling" method for determining fertilizer requirements of soils
AUTHOR(S): **Gunther, E.**
SOURCE: Z. Pflanzenernahr. Dungung (1926), B5, 32-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Critical expts. on Neubauer's method for determining the P2O5 and K requirements of soils show that considerable variations in the light intensity during growth of the seedlings affect the percentage of nutrients absorbed to a small extent only. Similarly, the absorption of nutrients by the seedlings is almost unaffected by changing the pH of a soil from an initial value of 5.0 to 6.5 and 8.0 by addition of CaCO3. Under normal conditions, both light intensity and soil reaction can be neglected in carrying out the test.

L17 ANSWER 66 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1924:17949 HCAPLUS
DOCUMENT NUMBER: 18:17949
ORIGINAL REFERENCE NO.: 18:2402h-i
TITLE: The lime-phosphoric acid factor in relation to the Aereboe-Wrangell system of fertilizing
AUTHOR(S): **Gunther, E.**
SOURCE: Z. Pflanzenernahr. Dungung (1924), 3B, 17-26
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Crops were treated with various fertilizers designed to produce neutral, acid and alkaline conditions in the soil but containing equivalent plant food. From the ratio CaO:P2O5 computed from analyses of the plant ash no division into classes appeared possible as proposed by Wrangell. Variations in the

amount and proportion of CaO and P2O5 occurred in different plants on the same soil and in the same species on different soils. Plants take up relatively more CaO than P2O5 under acid conditions than they do under basic ones.

L17 ANSWER 67 OF 67 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1913:9055 HCAPLUS
DOCUMENT NUMBER: 7:9055
ORIGINAL REFERENCE NO.: 7:1329c
TITLE: The Hoepfner Zinc Chloride Electrolytic Process
AUTHOR(S): **Gunther, E.**
SOURCE: Metall und Erz (1913), 1, 206-7
CODEN: MERZAG; ISSN: 0368-9514
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB G. describes briefly the development of the process under Eschellmann who succeeded in producing electrolytic Zn 99-97% pure.

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L5              STR
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L8              STR
L9          157 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L10             STR
L11          18 SEA FILE=REGISTRY SUB=L9 SSS FUL L10
L12           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L15          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("EMIG P"/AU OR "EMIG
                PETER"/AU)
L16          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 NOT L12
L17          67 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GUNTHER E"/AU OR "GUNTHER
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L18           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (("AUE B J"/AU OR "AUE
                BEATE"/AU)) NOT (L12 OR L16 OR L17)


=>
=>

=> d ibib abs l18 1

L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:408125 HCAPLUS
DOCUMENT NUMBER: 67:8125
TITLE: Fumarate reductase activity of Streptococcus faecalis
AUTHOR(S): Aue, B. J.; Deibel, Robert H.
CORPORATE SOURCE: Cornell Univ., Ithaca, NY, USA
SOURCE: Journal of Bacteriology (1967), 93(6), 1770-6
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Some characteristics of a fumarate reductase from S. faecalis are
described. The enzyme had a pH optimum of 7.4; optimal activity was
observed when the ionic strength of the phosphate buffer was adjusted to
0.088. The Km value of the enzyme for reduced flavine mononucleotide was
2 + 10-4M as determined with a 26-fold preparation In addition to fumarate,
the
enzyme reduced maleate and mesaconate. No succinate dehydrogenase
activity was detected, but succinate did act as an inhibitor of the
fumarate reductase activity. Other inhibitors were malonate, citraconate,
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and trans-,trans-muconate. Metal-chelating agents did not inhibit the enzyme. A limited inhibition by SH-binding agents was observed, and the prepns. were sensitive to air oxidation and storage. Glycine, alanine, histidine, and possibly lysine stimulated fumarate reductase activity in the cell-free exts. However, growth in media supplemented with glycine did not enhance fumarate reductase activity. The enzymic activity appears to be constitutive. 16 references.

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=> => d stat que l19 nos
L5              STR
L7       118852 SEA FILE=REGISTRY SSS FUL L5
L8              STR
L9          157 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L10             STR
L11          18 SEA FILE=REGISTRY SUB=L9 SSS FUL L10
L12           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L15          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("EMIG P"/AU OR "EMIG
                PETER"/AU)
L16          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 NOT L12
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L19          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (("POLYMEROPOULOS E"/AU OR
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                E"/AU)) NOT (L12 OR L16 OR L17 OR L18)


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L19  ANSWER 1 OF 41  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:53914  HCAPLUS
DOCUMENT NUMBER:          144:150233
TITLE:                    Preparation of 1,2,3,4-tetrahydrocarbazoles as
                          gonadotropin-releasing hormone receptor (LHRH)
                          antagonist
INVENTOR(S):              Paulini, Klaus; Gerlach, Matthias; Guenther, Eckhard;
                          Polymeropoulos, Emmanuel; Baasner, Silke;
                          Schmidt, Peter; Kuehne, Ronald; Soederhaell, Arvid
PATENT ASSIGNEE(S):       Zentaris G.m.b.H., Germany; Solvay Pharmaceuticals
                          B.V.
SOURCE:                   PCT Int. Appl., 113 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2006005484         A1    20060119    WO 2005-EP7255          20050705
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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|---|---|---|---|---|
| DE 102004033902 | A1 | 20060216 | DE 2004-102004033902 | 20040714 |
| US 2006014818 | A1 | 20060119 | US 2005-172142 | 20050630 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004033902A | 20040714 |
| | | | US 2004-587969P P | 20040714 |
| | | | US 2005-683178P P | 20050520 |

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X1 = S, O; X2, X3 = O with provisos; R1, R2 = H, aryl, alkyl, etc.; R3 = alkyl, arylalkyl, heteroarylalkyl, etc.; R4, R5, R6, R7 = H, halo, CN, etc.; R9 = H, alkyl, aryl, etc.; R10 = R11, COR11, CO2R11, etc.; R11 = alkyl, aryl, heteroaryl, etc.; R8 = alkylaryl, alkylheteroaryl, etc.; ] and their pharmaceutically acceptable salts were prepared For example, tetrahydrocarbazole II was prepared via solid phase synthesis from FmocValOH in 14% yield. In LHRH receptor binding assays, 7-examples of compds. I exhibited EC50 values ranging from 80-1.0 x 10-10 M.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:544300 HCAPLUS
DOCUMENT NUMBER: 143:146816
TITLE: Antagonist and agonist binding models of the human gonadotropin-releasing hormone receptor
AUTHOR(S): Soederhaell, J. Arvid; **Polymeropoulos, Emmanuel E.**; Paulini, Klaus; Guenther, Eckhard; Kuehne, Ronald
CORPORATE SOURCE: Institute for Molecular Pharmacology, Berlin, D-13125, Germany
SOURCE: Biochemical and Biophysical Research Communications (2005), 333(2), 568-582
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB G-protein-coupled receptors (GPCRs) constitute one of the most important classes of drug targets. Since the first high-resolution structure of a GPCR was determined by K. Palczewski and co-workers (2000), development of in silico models of rhodopsin-like GPCRs could be rationally founded. In this work, we present a model of the human gonadotropin-releasing hormone receptor based on the rhodopsin structure. The transmembrane helixes are modeled by homol., while the extra- and intracellular loops are modeled in such a way that exptl. determined interactions and microdomains (e.g., hydrophobic cores) are retained. We conclude that specifically tailored models, compared to more automatic approaches, have the benefit that known interactions are easily introduced early in the homol. modeling. Furthermore, tailored models, although more tedious to construct, are better suited for drug lead finding and for compound optimization. To test the stability of the receptor, we performed a 1 ns mol. dynamics simulation. Moreover, we docked two agonists (native GnRH and

Triptorelin) and two antagonists (Cetrorelix and the covalently constrained dicyclic decapeptide dicyclo(1,1'-5/4-10)[Ac-Glu1(Gly1')-DCpa2-DTrp3-Asp4-Dbu5-DNal6-Leu7-Arg8-Pro9-Dpr10-NH2]) into the putative receptor binding site. The docked ligand conformations result in ligand-receptor interactions that are generally in good agreement with site-directed mutagenesis and ligand-binding studies presented in the literature. Our results indicate that the binding conformation of the antagonists differs from that of the agonists. This difference can be linked to the activation or inhibition of the receptor.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:658086 HCAPLUS
DOCUMENT NUMBER: 137:185497
TITLE: Preparation of quinolines, isoquinolines and phthalazines as GnRH antagonists
INVENTOR(S): Strehlke, Peter; Droescher, Peter; Buehmann, Ulrich; Schmees, Norbert; Muhn, Peter; Hess-Stumpp, Holger; Kuehne, Roland; Guenther, Eckhard; **Polymeropoulos, Emmanuel**; Ter Laak, Antonius Marinus
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2002066437 | A1 | 20020829 | WO 2002-EP1882 | 20020221 |
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| DE 10108271 | A1 | 20020822 | DE 2001-10108271 | 20010221 |
| CA 2438709 | AA | 20020829 | CA 2002-2438709 | 20020221 |
| EP 1362034 | A1 | 20031119 | EP 2002-716803 | 20020221 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2002007451 | A | 20040601 | BR 2002-7451 | 20020221 |
| JP 2004528298 | T2 | 20040916 | JP 2002-565954 | 20020221 |
| NZ 527597 | A | 20041029 | NZ 2002-527597 | 20020221 |
| NO 2003003698 | A | 20031020 | NO 2003-3698 | 20030820 |
| BG 108165 | A | 20040831 | BG 2003-108165 | 20030909 |

| PRIORITY APPLN. INFO.: | | | |
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| | DE 2001-10108271 | A | 20010221 |
| | US 2001-274914P | P | 20010313 |
| | WO 2002-EP1882 | W | 20020221 |

OTHER SOURCE(S): MARPAT 137:185497
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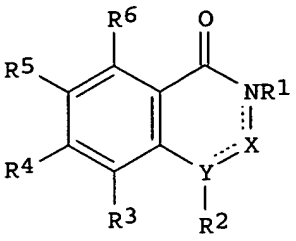

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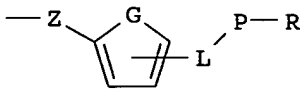

Q1

AB Title compds. [I; R1 = COR11, cyano, CO2R12, CONR12R13, etc.; R11, R12 = (saturated) (hetero)cyclyl, alkyl, (substituted) Ph, furanyl, thiophenyl; R13 = H, alkyl; R2 = CHR21R22, etc.; R21 = H, alkyl, (substituted) Ph; R22 = (substituted) Ph, naphthyl; R3 = H, alkyl; R4 = H, alkyl, halo; R5 = Q1; G = CH:CH, CH:N, N:CH, O, S; Z = bond, O, S, etc.; L = CH2, NH; P = CO, SOx; x = 0-2; R = (substituted) amino, (branched) (substituted) alkyl, 3-7 membered cycloalkyl; R6 = CH2NR61R62; R61 = H, alkyl; R62 = alkyl, (substituted) aralkyl], were prepared Thus, a mixture of N-benzylamine and N,N-diisopropylethylamine was added to 78 mg 6-(4-acetamidophenoxy)-5-(chloromethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid Et ester (preparation given) in DMF at 0° followed by stirring for 20 h at room temperature to give 70 mg 6-(4-acetamidophenoxy)-5-(N-benzyl-N-methylaminomethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid Et ester. The anal. of the antagonistic activity is given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:632477 HCAPLUS
DOCUMENT NUMBER: 137:154937
TITLE: Preparation of quinolines, isoquinolines and phthalazines as GnRH antagonists
INVENTOR(S): Strehlke, Peter; Droescher, Peter; Buehmann, Ulrich; Schmees, Norbert; Muhn, Peter; Hess-Stumpp, Holger; Kuehne, Roland; Guenther, Eckhard; **Polymeropoulos, Emmanuel**; Ter Laak, Antonius Marinus
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| DE 10108271 | A1 | 20020822 | DE 2001-10108271 | 20010221 |
| CA 2438709 | AA | 20020829 | CA 2002-2438709 | 20020221 |
| WO 2002066437 | A1 | 20020829 | WO 2002-EP1882 | 20020221 |

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| | BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| US 2003105328 | | A1 | 20030605 | US 2002-78530 | | 20020221 |
| US 6790858 | | B2 | 20040914 | | | |
| EP 1362034 | | A1 | 20031119 | EP 2002-716803 | | 20020221 |
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| | IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| CN 1496354 | | A | 20040512 | CN 2002-806359 | | 20020221 |
| BR 2002007451 | | A | 20040601 | BR 2002-7451 | | 20020221 |
| JP 2004528298 | | T2 | 20040916 | JP 2002-565954 | | 20020221 |
| NZ 527597 | | A | 20041029 | NZ 2002-527597 | | 20020221 |
| ZA 2003006429 | | A | 20040211 | ZA 2003-6429 | | 20030819 |
| NO 2003003698 | | A | 20031020 | NO 2003-3698 | | 20030820 |
| BG 108165 | | A | 20040831 | BG 2003-108165 | | 20030909 |
| US 2005004127 | | A1 | 20050106 | US 2004-896961 | | 20040723 |
| PRIORITY APPLN. INFO.: | | | | DE 2001-10108271 | A | 20010221 |
| | | | | US 2001-274914P | P | 20010313 |
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| | | | | WO 2002-EP1882 | W | 20020221 |

OTHER SOURCE(S): MARPAT 137:154937
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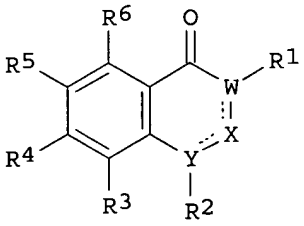

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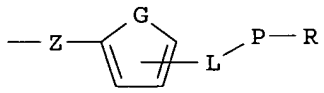

Q1

AB Title compds. [I; R1 = COR11, cyano, CO2R12, CONR12R13, etc.; R11, R12 = (saturated) cyclyl, heterocyclyl, alkyl, (substituted) Ph, furanyl, thiophenyl; R13 = H, alkyl; R2 = CHR21R22, etc.; R21 = H, alkyl, (substituted) Ph; R22 = (substituted) Ph, naphthyl; R3 = H, alkyl; R4 = H, alkyl, halo; R5 = Q1; G = C:C, C:N, N:C, O, S; Z = bond, O, S, etc.; L = CH2, NH; P = CO, SOx; x = 0-2; R = (substituted) amino, (branched) alkyl, 3-7 membered cycloalkyl; R6 = CH2NR61R62; R61 = H, alkyl; R62 = alkyl, (substituted) aralkyl, heteroarylalkyl, etc.], were prepared Thus, N-benzylamine and N,N-diisopropylethylamine was added to 78 mg 6-(4-acetamidophenoxy)-5-(chloromethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid Et ester (preparation given) in DMF at 0° followed by stirring for 20 h at room temperature to give 70 mg 6-(4-acetamidophenoxy)-5-(N-benzyl-N-methylaminomethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid Et ester. The anal. of the antagonistic activity is given.

L19 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:332190 HCAPLUS
DOCUMENT NUMBER: 136:340669
TITLE: Novel 7-azaindolecarboxamides as phosphodiesterase 4 inhibitors
INVENTOR(S): Hoefgen, Norbert; Egerland, Ute; Kronbach, Thomas;

Marx, Degenhard; Szelenyi, Stefan; Kuss, Hildegard;
**Polymeropoulos, Emmanuel**
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden Gmbh, Germany
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2002034747 | A1 | 20020502 | WO 2001-EP12376 | 20011025 |
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| DE 10053275 | A1 | 20020502 | DE 2000-10053275 | 20001027 |
| CA 2428468 | AA | 20020502 | CA 2001-2428468 | 20011025 |
| AU 2002021753 | A5 | 20020506 | AU 2002-21753 | 20011025 |
| EP 1330455 | A1 | 20030730 | EP 2001-988718 | 20011025 |
| EP 1330455 | B1 | 20050803 | | |
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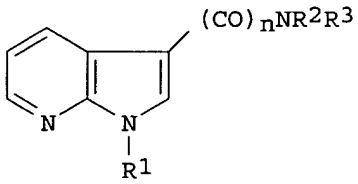
| EE 200300166 | A | 20030815 | EE 2003-166 | 20011025 |
| BR 2001014903 | A | 20031014 | BR 2001-14903 | 20011025 |
| JP 2004512337 | T2 | 20040422 | JP 2002-537738 | 20011025 |
| NZ 525369 | A | 20040924 | NZ 2001-525369 | 20011025 |
| AT 301121 | E | 20050815 | AT 2001-988718 | 20011025 |
| RU 2268887 | C2 | 20060127 | RU 2003-115621 | 20011025 |
| NO 2003001722 | A | 20030414 | NO 2003-1722 | 20030414 |
| BG 107725 | A | 20040831 | BG 2003-107725 | 20030416 |
| ZA 2003003236 | A | 20030731 | ZA 2003-3236 | 20030425 |
| HR 2003000427 | A1 | 20030831 | HR 2003-427 | 20030526 |
| US 2004106641 | A1 | 20040603 | US 2003-399051 | 20030617 |
| HK 1053839 | A1 | 20051028 | HK 2003-106201 | 20030829 |

PRIORITY APPLN. INFO.:
DE 2000-10053275 A 20001027
US 2000-244342P P 20001030
WO 2001-EP12376 W 20011025

OTHER SOURCE(S): CASREACT 136:340669; MARPAT 136:340669
GI




I

AB 7-Azaindoles I [n = 1, 2; R1 = (un)substituted alkyl, alkenyl; R2, R3 = H, (un)substituted alkyl, Ph, pyridyl, uracilyl, triazolyl; NR2R3 =

morpholino, thiomorpholino, thiomorpholine S,S-dioxide, 4-methylpiperazino] were prepared for use as PDE-4 inhibitors. Thus, 1-cyclopropylmethyl-7-azaindole-3-carboxylic acid was converted to the acid chloride and treated with 4-aminomethylpyridine to give the amide which had an IC50 for PDE-4 inhibition of 0.710 μmol./L.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:883023 HCAPLUS
DOCUMENT NUMBER: 134:360953
TITLE: A peptidic binding site model for PDE 4 inhibitors
AUTHOR(S): **Polymeropoulos, E. E.**; Hofgen, N.
CORPORATE SOURCE: Corporate R&D, ASTA Medica Group, Department of Chemical Research, Frankfurt, D-60314, Germany
SOURCE: Molecular Modeling and Prediction of Bioactivity, [Proceedings of the European Symposium on Quantitative Structure-Activity Relationships: Molecular Modeling and Prediction of Bioactivity], 12th, Copenhagen, Denmark, Aug. 23-28, 1998 (2000), Meeting Date 1998, 395-396. Editor(s): Gundertofte, Klaus; Jorgensen, Flemming Steen. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69ASO3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Selective inhibitors of the isoenzyme phosphodiesterase 4 (PDE 4) have attracted increased interest as potential drugs for the treatment of allergic diseases such as asthma. The pharmacophore requirements for inhibiting catalytic activity have been recently analyzed. To further refine this pharmacophore model and define a peptidic model for PDE 4 inhibitors that has the ability to semi-qual. predict inhibitory activity, the program PrGen has been used.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:567784 HCAPLUS
DOCUMENT NUMBER: 133:272153
TITLE: Langmuir Monolayers with Fluorinated Groups in the Hydrophilic Head. 1. Comparison of Trifluoroethyl Behenate and Ethyl Behenate Monolayers: Molecular Models, Mechanical Properties, Stability
AUTHOR(S): Petrov, J. G.; **Polymeropoulos, E. E.**; Moehwald, H.
CORPORATE SOURCE: Max-Planck Institute of Colloids and Interfaces, Golm/Potsdam, D-14476, Germany
SOURCE: Langmuir (2000), 16(19), 7411-7420
CODEN: LANGD5; ISSN: 0743-7463
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a series of three related papers we compare mech. properties and stability, morphol. and structure, and electrostatic potential and ellipsometric thickness of trifluoroethyl behenate (TFEB) and Et behenate (EB) Langmuir monolayers. The aim of these papers is to study the effect of fluorination of a Me group in the hydrophilic head on monolayer properties and structure. In the present Part 1 we show that trifluoroethyl ester forms significantly more unstable films with higher compressibility (lower compressional modulus) than the unsubstituted Et

ester. Both TFEB and EB surface pressure-area isotherms show compression-expansion hysteresis, but this hysteresis is larger for the fluorinated ester. The surface pressure-area loop of TFEB is shifted to larger mol. areas as compared to EB and gives larger limiting mol. areas at zero compression. This points to different vols. and/or conformations of the fluorinated and nonsubstituted hydrophilic heads. Maps of mol. lipophilicity and mol. electrostatic potential, based on semiempirical quantum mech. models of the two mols. in vacuo, relate the observed differences in monolayer properties to decreased hydrophilicity of the trifluoroethyl group and a stronger electrostatic repulsion between the hydrocarbon chains of TFEB. Such a repulsion results from polarization of the CH2 groups adjacent to the heads that is more significant for the trifluoroethyl behenate mol.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:55462 HCAPLUS
DOCUMENT NUMBER: 132:202635
TITLE: A peptidic binding site model for PDE 4 inhibitors
AUTHOR(S): **Polymeropoulos, Emmanuel E.**; Hofgen, Norbert
CORPORATE SOURCE: Department of Chemical Research, Corporate R and D ASTA Medica Group, Frankfurt, D-60314, Germany
SOURCE: Quantitative Structure-Activity Relationships (1999), 18(6), 543-547
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pseudoreceptor modeling program PrGen was used to construct a peptidic binding site model for phosphodiesterase 4 inhibitors. A training set of 21 diverse compds. (rolipram, nitraquazone and xanthine derivs., imidazo pyrido pyrazinones and 5-oxyindoles) was used to construct the binding site surrogate consisting of five amino acid residues, a Zn+2 cofactor and an envelope of charged virtual particles. The model was validated by predicting the free energies of binding ΔGpred0 of ten ligands (rolipram, imidazo pyrido pyrazinones and 5-oxyindoles). In seven cases the prediction was satisfactory. The rms deviation [4] in ΔG0 is 0.16 and 1.82 kcal/mol-resulting in an uncertainty in IC50 (or Ki) of 1.32 and 22.81-for the training and the test set resp., while the corresponding maximal prediction errors in ΔGpred0 were 0.27 kcal/mol and 4.50 kcal/mol.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:708761 HCAPLUS
DOCUMENT NUMBER: 131:310549
TITLE: New hydroxyindoles and their use as phosphodiesterase 4 and TNFα inhibitors
INVENTOR(S): Hofgen, Norbert; Egerland, Ute; Poppe, Hildegard; Marx, Degenhard; Szelenyi, Stefan; Kronbach, Thomas; **Polymeropoulos, Emmanuel**; Heer, Sabine
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9955696 | A1 | 19991104 | WO 1999-EP2792 | 19990424 |
| W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| DE 19818964 | A1 | 19991104 | DE 1998-19818964 | 19980428 |
| DE 19917504 | A1 | 20001019 | DE 1999-19917504 | 19990417 |
| AU 9938229 | A1 | 19991116 | AU 1999-38229 | 19990424 |
| AU 748403 | B2 | 20020606 | | |
| BR 9910029 | A | 20001226 | BR 1999-10029 | 19990424 |
| TR 200003130 | T2 | 20010122 | TR 2000-200003130 | 19990424 |
| EP 1076657 | A1 | 20010221 | EP 1999-920779 | 19990424 |
| EP 1076657 | B1 | 20040804 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002513017 | T2 | 20020508 | JP 2000-545856 | 19990424 |
| NZ 507406 | A | 20021126 | NZ 1999-507406 | 19990424 |
| RU 2217422 | C2 | 20031127 | RU 2000-129678 | 19990424 |
| AT 272631 | E | 20040815 | AT 1999-920779 | 19990424 |
| EP 1475377 | A1 | 20041110 | EP 2004-18391 | 19990424 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY | | | | |
| PT 1076657 | T | 20041130 | PT 1999-920779 | 19990424 |
| ES 2222706 | T3 | 20050201 | ES 1999-920779 | 19990424 |
| CA 2270301 | AA | 19991028 | CA 1999-2270301 | 19990428 |
| US 6251923 | B1 | 20010626 | US 1999-300973 | 19990428 |
| TW 530048 | B | 20030501 | TW 1999-88106886 | 19990428 |
| ZA 2000005540 | A | 20010327 | ZA 2000-5540 | 20001010 |
| BG 104842 | A | 20011031 | BG 2000-104842 | 20001011 |
| NO 2000005454 | A | 20001207 | NO 2000-5454 | 20001027 |
| HK 1035183 | A1 | 20050415 | HK 2001-105669 | 20010814 |
| US 2002111351 | A1 | 20020815 | US 2002-80821 | 20020221 |
| US 6545025 | B2 | 20030408 | | |
| US 2002115651 | A1 | 20020822 | US 2002-81395 | 20020221 |
| US 6545158 | B2 | 20030408 | | |
| US 2002119971 | A1 | 20020829 | US 2002-81642 | 20020221 |
| US 2002137745 | A1 | 20020926 | US 2002-81807 | 20020221 |
| US 6602890 | B2 | 20030805 | | |
| US 38624 | E | 20041012 | US 2002-176435 | 20020919 |
| US 2003134876 | A1 | 20030717 | US 2003-347659 | 20030120 |
| US 6613794 | B2 | 20030902 | | |
| US 2004220183 | A1 | 20041104 | US 2004-856034 | 20040527 |

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 1998-19818964 | A | 19980428 |
| | DE 1999-19917504 | A | 19990417 |
| | EP 1999-920779 | A3 | 19990424 |
| | WO 1999-EP2792 | W | 19990424 |
| | US 1999-300973 | A3 | 19990428 |
| | US 2000-653685 | A3 | 20000901 |
| | US 2002-81642 | A1 | 20020221 |
| | US 2002-81807 | A3 | 20020221 |

OTHER SOURCE(S): MARPAT 131:310549
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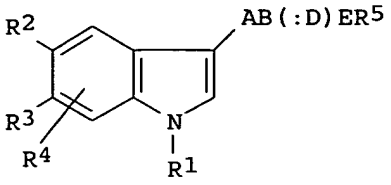


I

AB Hydroxyindoles I [R1, R5 = (un)substituted aliphatic, carbocyclic, heterocyclic, spirocyclic; R2, R3 = H, OH, ≥1 of them being OH; R4 = H, (un)substituted OH, SH, S(O)H, SO2H, NH2, CO2H, C(S)OH, NO2, CN, F, Cl, Br, I; A = alkylene, alkenylene, (CHOZ)m, CO, CS, C:NZ, O, S, NZ; Z = (un)substituted alkyl, alkenyl, carbocyclic, heterocyclic; B = C, S, SO; D = O, S, CH2, NZ; E = bond, (CH2)m, O, S, NZ; m = 0-3] were prepared I have IC50 for PDE IV inhibition of 1X10-9-1X10-5 and a selectivity relative to PDE's 2, 3, and 5 of 100-10,000. N-(3,5-dichloro-4-pyridyl)-2-[1-(4-fluorobenzyl)-5-methoxy-3-indolyl]-2-oxoacatamide was obtained by demethylation of the 5-methoxy compound and was reduced to the 2-hydroxyacetamide with NaBH4.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:469510 HCAPLUS
DOCUMENT NUMBER: 129:169977
TITLE: The real gordian knot. Racemic mixtures versus pure enantiomers
AUTHOR(S): Szelenyi, I.; Geisslinger, G.; **Polymeropoulos, E.**; Paul, W.; Herbst, M.; Brune, K.
CORPORATE SOURCE: Arzneimittelwerk Dresden, Radebeul, D-01445, Germany
SOURCE: Drug News & Perspectives (1998), 11(3), 139-160
CODEN: DNPEED; ISSN: 0214-0934
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 225 refs. is given on racemic mixts. and enantiomers of drugs. There are often pharmacodynamic, pharmacokinetic, and/or toxicol. differences between enantiomers. The choice between developing a racemate or single enantiomers depends on therapeutic advances and developmental costs involved. Regarding the target environment for drug intervention, even if natural physiol. mediators are achiral, their receptors may demonstrate a preference for the (-)- or (+)-enantiomer of agonists or antagonists. It is also obvious that the majority of enzymes and channels are stereospecific, at least to a variable extent. From a pharmacokinetics point of view, chirality can have an influence on drug absorption, distribution, metabolism, and elimination. With a few exceptions, toxicol. differences between isomers of known drugs are less dramatic than thought to be and only seldom substantiate the necessity of a racemic switch. The pharmaceutical industry is currently very interested in the so-called "racemic switch.". Before proceeding to a racemic switch it is necessary to determine if (1) it is chemical feasible to produce a single enantiomer, (2) a clin. advantage is obtainable through a racemic switch, and (3) a marketing advantage is obtainable. The real goal of a racemic switch should be the rational development of compds. that are profitable for the company and beneficial for the patient.

REFERENCE COUNT: 225 THERE ARE 225 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L19 ANSWER 11 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:744797 HCAPLUS
DOCUMENT NUMBER: 128:30427
TITLE: Chemistry and molecular biology in the search for new LHRH antagonists
AUTHOR(S): Kutscher, Bernhard; Bernd, Michael; Beckers, Thomas; **Polymeropoulos, Emmanuel E.**; Engel, Jurgen
CORPORATE SOURCE: ASTA Med. AG, Konzernforsch., Frankfurt, D-60315, Germany
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(20), 2149-2161
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 137 refs., discussing LHRH peptides as therapeutic agonists and antagonists of tumor growth, their structure and conformation, LHRH receptor assays, comparison of clin. relevant antagonists, LHRH receptor modeling, and the search for peptidomimetics for the LHRH receptor.
REFERENCE COUNT: 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 12 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:549055 HCAPLUS
DOCUMENT NUMBER: 127:229228
TITLE: A pharmacophore model for PDE IV inhibitors
AUTHOR(S): **Polymeropoulos, Emmanuel E.**; Hofgen, Norbert
CORPORATE SOURCE: ASTA Medica Group, Department Chemical Research, Frankfurt/Main, D-60314, Germany
SOURCE: Quantitative Structure-Activity Relationships (1997), 16(3), 231-234
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Based on conformational anal. and GRID-contour calcns. we developed a common primary pharmacophore for rolipram analog, nitraquazone and xanthine derivative PDE IV inhibitors. In spite of the structural differences exhibited by the three substance classes we could provide evidence that they share common hydrogen bonding and lipophilic enzyme binding sites.

L19 ANSWER 13 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:374503 HCAPLUS
DOCUMENT NUMBER: 125:104861
TITLE: D-23129: A new anticonvulsant with a broad spectrum activity in animal models of epileptic seizures
AUTHOR(S): Rostock, Angelika; Tober, Christine; Rundfeldt, Chris; Bartsch, Reni; Engel, Juergen; **Polymeropoulos, Emanuele E.**; Kutscher, Bernhard; Loescher, Wolfgang; Hoenack, Dagmar; et al.
CORPORATE SOURCE: ASTA Medica Group, Department Pharmacology, Radebeul, D-01445, Germany
SOURCE: Epilepsy Research (1996), 23(3), 211-223
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The anticonvulsant activity of the novel drug D-23129 (N-(2-amino-4-(4-fluorobenzylamino)phenyl)carbamic acid Et ester) was evaluated in animal models of epileptic seizures. D-23129 was active after oral and i.p. administration in rats and mice in a range of anticonvulsant tests at nontoxic doses. The compound was active against elec. induced seizures (MES, ED50 rat p.o. = 2.87 mg/kg), against seizures induced chemical by pentylenetetrazole (s.c. PTZ, ED50 mouse p.o. = 13.5 mg/kg), picrotoxin and N-methyl-D-aspartate (NMDA) and in a genetic animal model, the DBA/2 mouse. It was not active against seizures induced by bicuculline and strychnine. Motor impairment, evaluated with the rotarod test and by observation in the open field, was minimal at doses showing anticonvulsant activity. D-23129 was very effective in elevating the threshold for elec. and chemical induced seizures. Considering the dose increasing the MES threshold by 50% (TID50 mouse i.p. = 1.6 mg/kg; TID50 rat i.p. = 0.72 mg/kg) and the TD50 obtained in the rotarod test, the protective index of D-23129 is better than that of valproate and phenytoin. During 14 days chronic oral treatment with 15 mg/kg, no development of tolerance was observed D-23129 thus presents an orally active, safe, broad spectrum anticonvulsant agent, which is structurally unrelated to anticonvulsants currently used. We expect that D-23129 will improve the treatment of refractory seizures in humans.

L19 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:915127 HCAPLUS
DOCUMENT NUMBER: 123:305992
TITLE: Comparative Evaluation of the Predictive Power of Calculation Procedures for Molecular Lipophilicity
AUTHOR(S): Mannhold, Raimund; Rekker, Roelof F.; Sonntag, Christoph; Ter Laak, Anton M.; Dross, Karl; **Polymeropoulos, Emmanuel E.**
CORPORATE SOURCE: Department of Lasermedicine, Heinrich-Heine-Universitaet, Duesseldorf, 40225, Germany
SOURCE: Journal of Pharmaceutical Sciences (1995), 84(12), 1410-19
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The predictive power of four calcn. procedures for mol. lipophilicity is checked by comparing with exptl. data (log P and chromatog. RMw) taken from the literature. Two sets of test compds. are used: the first comprises simple organic mols. and the second consists of more complicated drug mols. Our comparative evaluation leads us to conclude that the predictive power is significantly better for not too complicated organic mols. than for drugs with complicated structural pattern. The four investigated calcn. procedures should be arranged in two groups with significantly differing predictive power: (a) Rekker and Hansch/Leo and (b) Ghose/Crippen and Suzuki/Kudo. This conclusion is based on a statistical control using log P and RMw as the independent parameters. Correlations have in common: (1) slopes in correlations with calculated data based on fragmental methods are not significantly different from 1; calcns. with data from atom-based procedures show up in most cases with slopes below 1. (2) The accompanying overall statistics underline the superiority of the fragmental methods. We think that all four tested calcn. procedures have their own restrictions; for future development we would advise a thorough reconsideration of structural effects not fully (or even not at all) incorporated in the data sets. Special attention will have to be paid to the conformational aspects of lipophilic behavior.

L19 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:663436 HCAPLUS
DOCUMENT NUMBER: 121:263436
TITLE: Chemical and Biological Evaluation of Hydrolysis Products of Cyclophosphamide
AUTHOR(S): Gilard, Veronique; Martino, Robert; Malet-Martino, Marie-C.; Kutscher, Bernhard; Mueller, Arndt; Niemeyer, Ulf; Pohl, Joerg; **Polymeropoulos, Emmanuel E.**
CORPORATE SOURCE: IMRCP Laboratory, Universite Paul Sabatier, Toulouse, 31062, Fr.
SOURCE: Journal of Medicinal Chemistry (1994), 37(23), 3986-93
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 31P NMR spectroscopy was used to study the products of the decomposition of cyclophosphamide (I) in buffered solns. at pH's ranging between 1.2 and 8.6 at 20° and at pH 7.4 at 37°. At pH 1.2, I undergoes a rapid breakdown (t1/2 = 1.4 days) of the 2 P-N bonds, giving [HN(CH2CH2Cl)2] and [H2N(CH2)3OP(O)(OH)2] as their hydrochlorides. No intermediates were detected. At pH's between 5.4 and 8.6, hydrolysis of I during 17 days led to the sole and previously unknown 9-membered ring compound (II). II resulted from the intramol. alkylation of I giving a bicyclic compound followed by the exothermal cleavage of the P-N bond in the 6-membered ring. At pH values ranging from 3.4 to 8.6, there is little degradation of I since more than 95% of initial I was still present after 7 days at 20°. Under physiol. conditions (pH 7.4, 37°) after 6 days, 45% of I was hydrolyzed (t1/2 = 6.6 days), leading essentially (30% of initial I) to II. The rate of hydrolysis of II and the nature of its hydrolysis products depended on pH over the range 0-8.6. After a single i.p. injection to mice, II, [H2N(CH2)3OP(O)(OH)2], and [Cl(CH2)2NH(CH2)2NH(CH2)3OP(O)(OH)2] were less toxic than I. They did not exhibit any direct cytotoxic efficacy on the colony-forming capacity of L1210 cells in vitro, and they had no antitumor activity in vivo against P388 leukemia.

L19 ANSWER 16 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:569732 HCAPLUS
DOCUMENT NUMBER: 121:169732
TITLE: GABAergic activity of triamino-pyridines and triamino-benzenes
AUTHOR(S): **Polymeropoulos, E. E.**; Kutscher, B.
CORPORATE SOURCE: ASTA Med. AG, Frankfurt, 6000, Germany
SOURCE: Trends QSAR Mol. Modell. 92, Proc. Eur. Symp. Struct.-Act. Relat.: QSAR Mol. Modell., 9th (1993), Meeting Date 1992, 456-60. Editor(s): Wermuth, Camille-Georges. ESCOM: Leiden, Neth.
CODEN: 59XTAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Electron d. distribution, isopotential surfaces, and mol. electrostatic potentials were determined for GABA agonists and antagonists. The program GRID was used to evaluate non-covalent drug-receptor interactions. Conformational anal. and structure optimization were also performed.

L19 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:625705 HCAPLUS
DOCUMENT NUMBER: 119:225705
TITLE: 1,2,4-triaminobenzene derivatives and a process for their preparation
INVENTOR(S): Dieter, Hans Reinhold; Engel, Juergen; Kutscher,

Bernhard; **Polymeropoulos, Emmanuel**;
Szelenyi, Stefan; Nickel, Bernd
PATENT ASSIGNEE(S): Asta Medica AG, Germany
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4200259 | A1 | 19930715 | DE 1992-4200259 | 19920108 |
| EP 554543 | A2 | 19930811 | EP 1992-121028 | 19921210 |
| EP 554543 | A3 | 19931027 | | |
| EP 554543 | B1 | 19960228 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| AT 134611 | E | 19960315 | AT 1992-121028 | 19921210 |
| ES 2084914 | T3 | 19960516 | ES 1992-121028 | 19921210 |
| CA 2086654 | AA | 19930709 | CA 1993-2086654 | 19930104 |
| CA 2086654 | C | 20030923 | | |
| ZA 9300011 | A | 19930805 | ZA 1993-11 | 19930104 |
| JP 05345752 | A2 | 19931227 | JP 1993-1054 | 19930107 |
| JP 3145220 | B2 | 20010312 | | |
| US 5384330 | A | 19950124 | US 1993-2458 | 19930108 |

PRIORITY APPLN. INFO.: DE 1992-4200259 A 19920108
OTHER SOURCE(S): CASREACT 119:225705; MARPAT 119:225705
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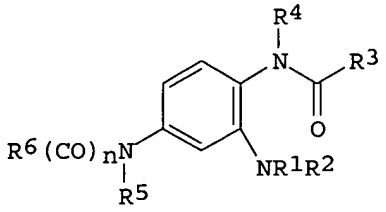


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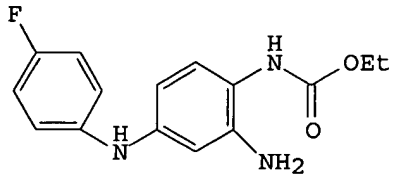


II

AB The title compds., 2-amino-1,4-bis(acylamino)benzene derivs. I (R1 = hydrogen, alkyl, etc.; R3 = alkoxy, amino, etc.; R4, R5 = hydrogen, alkyl; R6 = arylalkyl) and pharmaceuticals containing them are claimed. I are anticonvulsants, antipyretics, antiepileptics, muscle relaxants, and peripheral analgesics. Some I were tested as antiepileptics in electroshock-induced convulsions in rats. Reductive carbamoylation of 2-amino-4-[(4-fluorobenzy)amino]-1-nitrobenzene gave 2-amino-4-[(4-fluorobenzyl)amino]-1-[(ethoxycarbonyl)amino]benzene [ethyl [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]carbamate] (II); II dihydrochloride was obtained in 73% yield.

L19 ANSWER 18 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:594860 HCAPLUS
DOCUMENT NUMBER: 119:194860
TITLE: l-Deprenyl: A unique MAO-B inhibitor
AUTHOR(S): **Polymeropoulos, E. E.**
CORPORATE SOURCE: Dep. Sci. Inf., ASTA Med. A.-G., Frankfurt/Main, Germany
SOURCE: Inhib. Monoamine Oxidase B (1993), 109-24. Editor(s):

Szelenyi, Istvan. Birkhaeuser: Basel, Switz.
CODEN: 59HWAP
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 32 refs.

L19 ANSWER 19 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:622766 HCAPLUS
DOCUMENT NUMBER: 115:222766
TITLE: Computer-assisted analysis of the possible binding sites of H1-antagonists
AUTHOR(S): **Polymeropoulos, E. E.**; Kutscher, B.; Fleischhauer, I.
CORPORATE SOURCE: ASTA Pharma A.-G., Frankfurt, D-6000/1, Germany
SOURCE: Pharmacochemistry Library (1991), 16(QSAR: Ration. Approaches Des. Bioact. Compd.), 761-4
CODEN: PHLIDQ; ISSN: 0165-7208
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of antiallergic-antihistaminic compds. acting as H1-receptor antagonists was analyzed with regard to their structural and electronic properties by means of the quantum mech. methods and the program GRID. A model defining possible common binding sites is suggested.

L19 ANSWER 20 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:227015 HCAPLUS
DOCUMENT NUMBER: 108:227015
TITLE: Structure and dynamics of noble gas clusters and cluster ions
AUTHOR(S): Brickmann, J.; **Polymeropoulos, E. E.**; Meisel, D.
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Contrib. - Symp. At. Surf. Phys. (1986), 342-9.
Editor(s): Howorka, F.; Lindinger, W.; Maerk, T. D.
Inst. Atomphys. Univ. Innsbruck: Innsbruck, Austria.
CODEN: 56GBA4
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 15 refs. is given of authors own and related work.

L19 ANSWER 21 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:529434 HCAPLUS
DOCUMENT NUMBER: 103:129434
TITLE: Magic numbers in ionized rare-gas clusters
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chemie, Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Surface Science (1985), 156(2), 563-71
CODEN: SUSCAS; ISSN: 0039-6028
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relative stability of ionized rare-gas clusters Xn+, with n = 5-20 for Arn+ and n = 5-26 for Xen+ was studied by means of a combined mol. dynamics and Monte Carlo technique. Stable ionized clusters with "magic nos." n = 19 for Ar and n = 13, 19 and 25 for Xe occur, in agreement with exptl. time-of-flight mass spectra.

L19 ANSWER 22 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:518290 HCAPLUS

DOCUMENT NUMBER: 103:118290
TITLE: Molecular dynamics of ion transport through transmembrane model channels
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Annual Review of Biophysics and Biophysical Chemistry (1985), 14, 315-30
CODEN: ARBCEY; ISSN: 0883-9182
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 101 refs., of mol. dynamics of ion transport through transmembrane model channels (i.e., ionophore channels), including the use of simulation methods to describe processes involved in these systems.

L19 ANSWER 23 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:442966 HCAPLUS
DOCUMENT NUMBER: 103:42966
TITLE: The stability of rare gas clusters by ionization
AUTHOR(S): **Polymeropoulos, E. E.**; Loeffler, S.; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hoch. Darmstadt, Darmstadt, D 6100, Fed. Rep. Ger.
SOURCE: Zeitschrift fuer Naturforschung, Teil A: Physik, Physikalische Chemie, Kosmophysik (1985), 40A(5), 516-19
CODEN: ZTAKDZ; ISSN: 0340-4811
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Computer simulations were made of the dissociation dynamics of Ar and Xe neutral and singly-charged clusters with 5-20 atoms. The stability of clusters with magic nos. (P. and B., 1983) of atoms (n = 19 for Ar, and n = 13, 19 for Xe), as found in time-of-flight mass spectra (J. Farges, et al., 1983), was greater for the ionized clusters than for the neutral clusters, indicating the importance of ionization on the cluster-size distribution found in expts.

L19 ANSWER 24 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:442961 HCAPLUS
DOCUMENT NUMBER: 103:42961
TITLE: Molecular-dynamics simulations in systems of rare gases using Axilrod-Teller and exchange three-atom interactions
AUTHOR(S): **Polymeropoulos, E. E.**; Bopp, P.; Brickmann, J.; Jansen, L.; Block, R.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1985), 31(6), 3565-9
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By using previous results (P., et al., 1984), mol.-dynamics simulations of cluster formation in compressed Ar and Xe gases were done with a Lennard-Jones (6,12) potential, Axilrod-Teller 3-atom interactions, and exchange-type interactions. Selective stabilization of the clusters Ar19, Xe13, and Xe19 (possibly also Xe25) was established, predominantly as a result of the 3-atom exchange potential. These exchange contributions, in combination with selective stability due to cluster ionization, can explain the phenomena observed in existing time-of-flight mass-spectroscopy

expts. on rare-gas-atom clusters.

L19 ANSWER 25 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:144899 HCAPLUS
DOCUMENT NUMBER: 102:144899
TITLE: Solvent effects in ionic transport through transmembrane protein channels
AUTHOR(S): Kappas, U.; Fischer, W.; **Polymeropoulos, E. E.** ; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-1600, Fed. Rep. Ger.
SOURCE: Journal of Theoretical Biology (1985), 112(3), 459-64
CODEN: JTBIAP; ISSN: 0022-5193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ion transport through a gramicidin A-like channel in the presence of solvent mols. with van der Waals parameters of H2O was studied by means of mol. dynamics simulation. The presence of solvent mols. in the channel tended to equalize the effective masses of ions through association, thus predicting the exptl. observed ion selectivity of the gramicidin A channel.

L19 ANSWER 26 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:119844 HCAPLUS
DOCUMENT NUMBER: 102:119844
TITLE: Exchange perturbation theory calculations of the interaction energy between two ground-state hydrogen atoms
AUTHOR(S): Adams, William H.; Clayton, Meredith M.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Dep. Chem., Rutgers Univ., New Brunswick, NJ, 08903, USA
SOURCE: International Journal of Quantum Chemistry, Quantum Chemistry Symposium (1984), 18, 393-406
CODEN: IJQSDI; ISSN: 0161-3642
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of calcns. were made of the interaction energy between two H atoms in their ground states, using three kinds of exchange perturbation theory. One objective was to test the accuracy that could be achieved with these perturbation methods. A second was to see if the results were consistent with those for H2+. The perturbation equations were solved within the CI approximation, using 226 partially symmetry-contracted, two-electron basis functions. The set of Slater-type basis orbitals was chosen so that we could approx. within 2% the most accurate calculated interaction energies. The second-order energies were reported at a series of nuclear separation and compare them to the best values that have been published. Some of the published values are inaccurate. The % errors in the interaction energies approximated by summing through second and third orders were given.

L19 ANSWER 27 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:577869 HCAPLUS
DOCUMENT NUMBER: 101:177869
TITLE: Analysis of three-body potentials in systems of rare-gas atoms: Axilrod-Teller versus three-atom exchange interactions
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.; Jansen, L.; Block, R.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.

SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1984), 30(4), 1593-9
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The triple-dipole (Axilrod-Teller) and the exchange 3-atom potentials were compared for a number of specific arrangements of 3 argon atoms and 3 xenon atoms. For these configurations, total potentials were constructed, taking a Lennard-Jones (6-12) potential for each pair. For all arrangements, the exchange 3-atom potential was the most important correction to the two-body interaction. Qual., the changes with respect to the 2-body potential were more pronounced for Xe than for Ar.

L19 ANSWER 28 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:57103 HCAPLUS
DOCUMENT NUMBER: 100:57103
TITLE: The influence of three-body forces on the lifetime and stability of rare gas clusters
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1983), 87(12), 1190-5
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of clusters in compressed Ar and Xe gases is studied with the mol. dynamics simulation technique using 2-body Lennard-Jones and 3-body Axilrod-Teller interaction potentials. The effect of 3-body interactions is a function of the temperature of the system and increases with decreasing temperature The occurrence of clusters corresponding to the "magic-number" n = 13 for Xe is explained in terms of the dispersion forces inherent in the Axilrod-Teller potential. Computer generated images of stable and unstable Xe13 clusters are presented.

L19 ANSWER 29 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:185974 HCAPLUS
DOCUMENT NUMBER: 98:185974
TITLE: On the origin of the occurrence of "magic numbers" in cluster size distributions of xenon in the compressed gas phase
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Chemical Physics Letters (1983), 96(3), 273-5
CODEN: CHPLBC; ISSN: 0009-2614
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of clusters in compressed Ar and Xe is studied with the mol. dynamics simulation technique using 2-body Lennard-Jones and 3-body Axilrod-Teller potentials. The occurrence of clusters corresponding to the "magic number" n = 13 for Xe and the absence of such stable clusters for Ar is due to the dispersion forces that result from triplet-dipole interaction.

L19 ANSWER 30 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:623356 HCAPLUS
DOCUMENT NUMBER: 97:223356
TITLE: Molecular dynamics study of the formation of argon clusters in the compressed gas

AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Techn. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Chemical Physics Letters (1982), 92(1), 59-63
CODEN: CHPLBC; ISSN: 0009-2614
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of clusters (nucleation) in compressed Ar gas was studied via mol.-dynamics simulation with 2-body Lennard-Jones and 3-body Axilrod-Teller potentials. The 3-body interactions become increasingly important, with decreasing temperature, for cluster stability and cluster size distributions.

L19 ANSWER 31 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:93471 HCAPLUS
DOCUMENT NUMBER: 94:93471
TITLE: Photoinitiated electron transfer between donors and acceptors in monomolecular layer assemblies - EPR and optical studies
AUTHOR(S): Cunningham, J.; **Polymeropoulos, E. E.**; Moebius, D.; Baer, F.
CORPORATE SOURCE: Max Planck-Inst. Biophys. Chem., Goettingen, D 3400, Fed. Rep. Ger.
SOURCE: NATO Advanced Study Institutes Series, Series C: Mathematical and Physical Sciences (1980), 61(Magn. Reson. Colloid Interface Sci.), 603-8
CODEN: NASCD6; ISSN: 0377-2071
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies were made by EPR and fluorescence quenching (FQ) techniques of factors influencing photoinitiated electron transfer from donor species organized as one monomol. layer towards acceptor mols. located 20 Å distant in another monomol. layer. Whenever a paraquat type acceptor was incorporated, illumination at wavelengths absorbed by different cyanine or porphyrin donors yielded a weak anisotropic EPR signal consistent with formation of appropriately aligned alkyl-viologen radicals by electron trapping. Time scale and efficiency of EPR signal growth, allied to dependence on thickness of the spacing monolayer, differed markedly from characteristics of FQ. Implications of these differences for relative rates of processes following photoinitiated charge separation in the monolayer assemblies are considered.

L19 ANSWER 32 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:642620 HCAPLUS
DOCUMENT NUMBER: 93:242620
TITLE: Monolayer assemblies with functional units of sensitizing and conducting molecular components: photovoltage, dark conduction and photoconduction in systems with aluminum and barium electrodes
AUTHOR(S): **Polymeropoulos, E. E.**; Moebius, D.; Kuhn, H.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, D 3400, Fed. Rep. Ger.
SOURCE: Thin Solid Films (1980), 68(1), 173-90
CODEN: THSFAP; ISSN: 0040-6090
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vectorial change separation was studied in assemblies in which a mixed monolayer of an indocarbocyanine dye with the chromophores in the layer plane, a chain-like $\pi$ electron system oriented perpendicular to the layer plane, and a layer of acceptor mols. were sandwiched between metal

electrodes. The cyanine dye was excited by light, and the excited electron could move via the π electron system and the acceptor to the pos. biased electrode. If these arrangements are sandwiched between metals of very different work functions (Al and Ba), a photovoltage can be measured and is interpreted as being caused by a vectorial electron transfer through the mol. functional unit towards the metal with the smaller work function. The dark conductivity through fatty acid multilayers sandwiched between an Al and a Ba electrode was measured and was interpreted. The hopping of electrons between interlayer states adjacent to the Al electrode is rate-limiting.

L19 ANSWER 33 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:224221 HCAPLUS
DOCUMENT NUMBER: 92:224221
TITLE: Photochromism in monolayers
AUTHOR(S): **Polymeropoulos, E. E.**; Moebius, D.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, D-3400, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1979), 83(12), 1215-22
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The photochromic properties of 1'-octadecyl-3',3'-dimethyl-6-nitropiro[2H-1-benzopyran-2,2'-indoline](I) were studied in monolayers at the air-H2O interface by measuring the surface pressure-area isotherms and the surface potential of several mixts. of I with tripalmitine. By using the Langmuir-Blodgett technique, mixed monolayers of tripalmitine and I in a molar mixing ratio of 6:1 were transferred onto glass slides and their photochromic properties in monolayer assemblies were studied.

L19 ANSWER 34 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:203868 HCAPLUS
DOCUMENT NUMBER: 92:203868
TITLE: Exchange perturbation theory. IV. Calculations on diatomic hydrogen (H) ion
AUTHOR(S): Adams, William H.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Dep. Chem., Rutgers, State Univ., New Brunswick, NJ, 08903, USA
SOURCE: Journal of Chemical Physics (1980), 72(5), 2981-9
CODEN: JCPSA6; ISSN: 0021-9606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Authors have applied the two localized-wave-functions (LW) exchange-perturbation-theories (EPT) which they have proposed (1978) to the 1sσg and 2pσu states of H2+ with the objective of verifying the insights gained from these EPT's and testing their accuracy. The one LW EPT dets. a primitive wave function identical to that of the Eisenschitz-London EPT through first order, but which differs from it in all higher orders. The other dets. a function identical to that of the Hirschfelder-Silbey EPT through first order and through infinite order, but which differs from it through all intermediate orders. In terms of the perturbation expansion of the interaction energy through third order, authors' EPT's are as accurate as the original EPT's to which they are related. The LW EPT's have the conceptual asset that their primitive wave functions are least distorted from the zero order wave function in a precisely defined sense. Interaction energies were also calculated using the integrals which define the interaction energies in terms of LW's, and substituting the LW's approximated by sums through first, second, and third order. The energies generally increase in accuracy as the LW is

summed to higher orders. When each order contribution to the LW is multiplied by a weight which is determined to minimize the interaction energy, and the LW is summed through third order, the interaction energy is in error by 0.07% or less for nuclear sepns. ranging from 1.0 to 10.0 bohr. An examination of the LW's shows how the optimization procedure works. Other quantities are calculated which show that the LW EPT's are systematically refinable methods for the calcn. of LW's as well as for the calcn. of interaction energies. This is important because LW'S may be used to calculate distinct "phys." contributions to interaction energies.

L19 ANSWER 35 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:131519 HCAPLUS
DOCUMENT NUMBER: 90:131519
TITLE: Electron tunneling through superconducting aluminum/monolayer/lead junctions
AUTHOR(S): **Polymeropoulos, E. E.**
CORPORATE SOURCE: Abt. Mol. Syst., Mas-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Solid State Communications (1978), 28(10), 883-5
CODEN: SSCOA4; ISSN: 0038-1098
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The current-voltage characteristics of Al/adsorbed monolayer/Pb junctions was determined at 77, 4.2, and 1.8 K for applied voltages 1-3 mV. At 77 K the current changes linearly with voltage whereas at 4.2 and 1.8 K the relation becomes nonlinear. Based on results at 1.8 K, an approx. band gap for Pb equal to 2.6 meV was obtained. The observation of a nonlinear current-voltage characteristic at temps. where Pb becomes superconducting is strong evidence that the observed current through the insulator is a tunneling current.

L19 ANSWER 36 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:589545 HCAPLUS
DOCUMENT NUMBER: 89:189545
TITLE: Electrical conduction through adsorbed monolayers
AUTHOR(S): **Polymeropoulos, E. E.**; Sagiv, J.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Journal of Chemical Physics (1978), 69(5), 1836-47
CODEN: JCPSA6; ISSN: 0021-9606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Elec. conduction was studied in Al/adsorbed monolayer/Al junctions. The adsorbed monolayers were long chain saturated fatty acids (23-14 C atom chain), short chain perfluorinated fatty acids (10-7 C atom chain), and n-octadecyltrichlorosilane. The current observed decreased rapidly with decreasing temperature from 295 K to .apprx.77 K at which point the decrease in current with decreasing temperature became very small. At room temperature (295 K) there was no definite relation between the d.c. conductivity and the length of the fatty acids. At ≤77 K, however, the d.c. conductivity was exponentially dependent on the fatty-acid chain length. Thus, at ≤77 K the conduction mech. is tunneling through the monolayer. The tunneling barrier height was of the order of 2.8 and 5.2 eV for fatty acids and perfluorinated fatty acids, resp. By artificially producing mol. holes in monolayers, in the presence of such holds it was shown, the current increases by at least one order of magnitude while the effective barrier height is lowered by 10%. Differences between the present results and those previously obtained with monolayers deposited from an air-water

interface (Langmuir-Blodgett monolayer) are discussed.

L19 ANSWER 37 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:569628 HCAPLUS
DOCUMENT NUMBER: 89:169628
TITLE: Adsorbed monolayers. Molecular organization and electrical properties
AUTHOR(S): Sagiv, J.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Max-Planck-Inst. Biophys. Chem., Karl-Friedrich-Bonhoeffer-Inst., Goettingen-Nikolausberg, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1978), 82(9), 882
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adsorption was used to obtain monolayers with a controllable mol. organization. The adsorption process and structure of dye-containing monolayers were studied by spectroscopy. Adsorbed monolayers were used in study of elec. conductivity through organic films. Oleophobic monolayers of long-chain surfactants and mixed monolayers containing dyes were studied. Octadecyltrichlorosilane (OTS) was used as an adsorbate-adsorbent bonding agent. Mol-holes were produced in OTS + dye monolayers by removal of the dye. Addition of other mols. to those holes gives a type of mol. organization. Anisotropic mol. distributions were induced in monolayers by adsorption on oriented polymeric surfaces. The elec. properties (capacitance, current, tunneling, and dielec. constant) were studied of adsorbed monolayers on Al electrodes. These adsorbed monolayers included fatty acids, perfluorinated fatty acids, and OTS. Adsorbed monolayers may be used as insulators in Al/monolayer Pb superconducting tunneling junctions.

L19 ANSWER 38 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:435174 HCAPLUS
DOCUMENT NUMBER: 89:35174
TITLE: Photoconduction in monolayer assemblies with functional units of sensitizing and conducting molecular components
AUTHOR(S): **Polymeropoulos, E. E.**; Moebius, D.; Kuhn, H.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Journal of Chemical Physics (1978), 68(8), 3918-31
CODEN: JCPSA6; ISSN: 0021-9606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vectorial charge separation was studied in assemblies where a mixed monolayer of a cyanine dye with the chromophores in the layer plane and a chainlike $\pi$-electron system oriented perpendicular to the layer plane are sandwiched between fatty acid monolayers and metal electrodes. The cyanine dye is excited by light, and the excited electrons move through the $\pi$-electron system which acts as the conducting element. Conduction takes place according to different mechanisms depending on the temperature In the low-temperature mode the logarithm of the photocurrent decreases linearly with (1/T)1/2, while in the high-temperature mode it decreases linearly with 1/T; in both modes the photocurrent is proportional to the light intensity and its logarithm increases linearly with the bias voltage. If the conducting $\pi$-electron system is absent, the photocurrent is about an order of magnitude smaller but again proportional to the light intensity. Its logarithm increases linearly with the square root of the bias voltage. The results in the complex assembly can be interpreted by assuming that the excited electron is transfered from the cyanine dye to the

π-electron system by tunneling or by thermal activation over a barrier of 0.25 eV; from there it tunnels through the next fatty acid layer to an interface state, and then hops to the pos. biased electrode. This model can be checked by specifically altering the thickness of the tunneling barrier (by exchanging arachidic acid for fatty acids with shorter chain lengths). In the arrangement where the conducting element is absent, the results are interpreted by assuming that the excited electron either tunnels through or is thermally activated over the potential barrier of the hydrocarbon matrix (1 eV). The different voltage dependence in the two arrangements with and without the conducting π-electron system can be quant. explained as being due to the fact that the chromophore of the cyanine dye is perpendicular to the applied field, while the chain of the π-electron system is parallel to this field.

L19 ANSWER 39 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:126608 HCAPLUS
DOCUMENT NUMBER: 88:126608
TITLE: Exchange perturbation theory. III. Hirschfelder-Silbey type
AUTHOR(S): **Polymeropoulos, E. E.**; Adams, William H.
CORPORATE SOURCE: Sch. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1978), 17(1), 24-9
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An exchange perturbation theory is developed which yields in infinite order the same primitive function F that is found in infinite order with the Hirschfelder-Silbey (HS) theory. The perturbation equations are identical to the HS equations only through first order. This is because the perturbing potential in our theory is not the bare interaction potential of the HS theory, but rather that potential screened by a nonlocal potential. The screening is the weakest that we have found in studying the equations satisfied by primitive functions, which are least distorted from products of the functions for the subsystems when the interactions have been turned off. It is argued that this HS-type theory is best used when the interactions are weak.

L19 ANSWER 40 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:126607 HCAPLUS
DOCUMENT NUMBER: 88:126607
TITLE: Exchange perturbation theory. II. Eisenschitz-London type
AUTHOR(S): **Polymeropoulos, E. E.**; Adams, William H.
CORPORATE SOURCE: Sch. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1978), 17(1), 18-23
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An exchange perturbation theory is developed which is identical through first order in the primitive function G with the Eisenschitz-London (EL) theory. In higher orders, G is different from the EL primitive function and from the primitive functions of related theories. The function G is least distorted from the zeroth-order function F0, a product of functions for the subsystems when the interactions have been set equal to zero. The potential which distorts F0 into G is more thoroughly screened than in any other theory we have examined This EL-type theory should be used when the

unscreened interactions are strong.

L19 ANSWER 41 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:126606 HCAPLUS
DOCUMENT NUMBER: 88:126606
TITLE: Exchange perturbation theory. I. General definitions and relations
AUTHOR(S): Adams, William H.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Sch. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1978), 17(1), 11-17
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A class of primitive functions are defined which are least distorted from the unsymmetrized function F0, a product of atomic or other group functions, in the limit that the interactions between the groups have been turned off. These primitive functions have the property that at least one Schroedinger eigenfunction may be obtained from them by sym. projection. The screened potential is regarded as a perturbation and the corresponding Rayleigh-Schroedinger perturbation equations are derived. It is shown that a number of inequivalent, but equally valid energy expressions may be defined in terms of the primitive functions. Only when the primitive function is calculated exactly to infinite order will the different energy expressions all yield the same numerical value. It is suggested that this provides a check on the accuracy of approx. primitive functions.

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=> => d stat que l20 nos
L5              STR
L7       118852 SEA FILE=REGISTRY SSS FUL L5
L8              STR
L9          157 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L10             STR
L11          18 SEA FILE=REGISTRY SUB=L9 SSS FUL L10
L12           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L15          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("EMIG P"/AU OR "EMIG
                PETER"/AU)
L16          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 NOT L12
L17          67 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GUNTHER E"/AU OR "GUNTHER
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L18           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (("AUE B J"/AU OR "AUE
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L19          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (("POLYMEROPOULOS E"/AU OR
                "POLYMEROPOULOS E E"/AU OR "POLYMEROPOULOS EMANUELE E"/AU OR
                "POLYMEROPOULOS EMMANUEL"/AU OR "POLYMEROPOULOS EMMANUEL
                E"/AU)) NOT (L12 OR L16 OR L17 OR L18)
L20          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (("BAASNER S"/AU OR "BAASNER
                SIIKE"/AU OR "BAASNER SILKE"/AU)) NOT (L12 OR L16 OR L17 OR
                L18 OR L19)


=> d ibib abs l20 1-12

L20 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1261687 HCAPLUS
DOCUMENT NUMBER: 144:22948
TITLE: Preparation of fused indoles as anticancer drugs.
INVENTOR(S): Weinberger, Heinz; Beckers, Thomas; Schmidt, Mathias;
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| | |
|---|---|
| | **Baasner, Silke**; Nickel, Bernd |
| PATENT ASSIGNEE(S): | Zentaris AG, Germany; Zentaris GmbH |
| SOURCE: | U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 233,135. |
| | CODEN: USXXCO |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 2 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2005267303 | A1 | 20051201 | US 2005-136688 | | 20050524 |
| US 2004039197 | A1 | 20040226 | US 2002-233135 | | 20020830 |
| PRIORITY APPLN. INFO.: | | | US 2001-317102P | P | 20010904 |
| | | | US 2002-233135 | A2 | 20020830 |
| | | | DE 2001-10143079 | A | 20010903 |

OTHER SOURCE(S): MARPAT 144:22948

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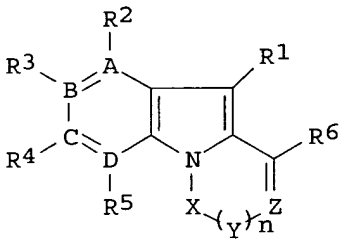

I

AB The invention relates to novel, substituted, fused indole and heteroindole derivs. of the general formula I their tautomers, stereoisomers, mixts. and pharmaceutically acceptable salts, their synthesis and their use as pharmaceuticals, especially as anti-tumor agents, for mammals, especially for man.

Title compds. [I; R1 = H, (substituted) aryl, heteroaryl, cycloalkyl, alkyl; A, B, D, E = substituted C; R2-R5 = H, halo, cyano, NO2, OH, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylcarbonyloxy, alkylsulfonyl, CO2H, amino, etc.; R6 = (substituted) aryl, heteroaryl, cycloalkyl, alkyl, alkoxy; X = CO; n = 0 ], were prepared Thus, reaction of 1H-indole-2-ylmethanone oxime Ph methanone oxime (preparation given) with carbonyldiimidazole in refluxing THF gave (5-methoxy-1H-indole-2-yl)phenylmethanone oxime. This at 3.16 μg/mL showed 90.7% antiproliferative activity against HeLa/KB in an XTT cytotoxicity test.

L20 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2005:141028 HCAPLUS |
| DOCUMENT NUMBER: | 142:240315 |
| TITLE: | Preparation of indolyl-3-glyoxylic acid amides for the treatment of tumors |
| INVENTOR(S): | Gerlach, Matthias; Schuster, Tilmann; Schmidt, Peter; **Baasner, Silke**; Guenther, Eckhard |
| PATENT ASSIGNEE(S): | Zentaris G.m.b.H., Germany |
| SOURCE: | PCT Int. Appl., 25 pp. |
| | CODEN: PIXXD2 |

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005014542 | A2 | 20050217 | WO 2004-EP7573 | 20040709 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10334040 | A1 | 20050310 | DE 2003-10334040 | 20030725 |

PRIORITY APPLN. INFO.: DE 2003-10334040 A 20030725
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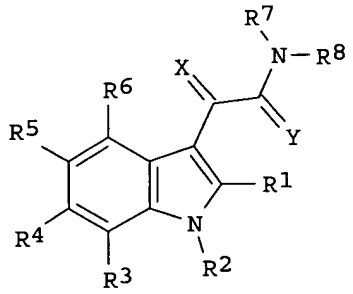


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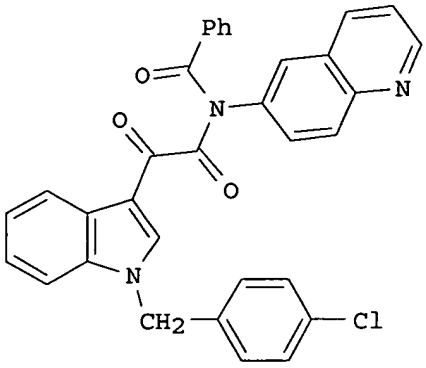


II

AB Title compds. I [R1, R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, aryl, etc.;R7 = SO2X1, COX2, COOX3, etc.; X1 = N(alkyl)2, OH, (un)substituted alkyl, etc.; X2 = (un)substituted aryl, heteroaryl, alkylaryl, etc.; X3 = (un)substituted cycloalkyl, heterocyclyl, aryl, etc.; R8 = Het; X = O, S with provisos; Y = O, S] and their

pharmaceutically acceptable salts were prepared In human cervical cancer cell line (KB/HeLa) antiproliferative assay, indolylglyoxylic acid amide II exhibited an IC50 value of 0.170 μg/mL. Compds. I are claimed to be useful for the treatment of tumors.

L20 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:885644 HCAPLUS
DOCUMENT NUMBER: 140:26268
TITLE: Switching Off HER-2/neu in a Tetracycline-Controlled Mouse Tumor Model Leads to Apoptosis and Tumor-Size-Dependent Remission
AUTHOR(S): Schiffer, Ilka B.; Gebhard, Susanne; Heimerdinger, Carolin K.; Heling, Annette; Hast, Jochem; Wollscheid, Ursula; Seliger, Barbara; Tanner, Berno; Gilbert, Sandra; Beckers, Thomas; **Baasner, Silke**; Brenner, Walburgis; Spangenberg, Christian; Prawitt, Dirk; Trost, Tatjana; Schreiber, Wolfgang G.; Zabel, Bernhard; Thelen, Manfred; Lehr, Hans-Anton; Oesch, Franz; Hengstler, Jan G.
CORPORATE SOURCE: Departments of Radiology, Institute of Toxicology, University of Mainz, Mainz, 55131, Germany
SOURCE: Cancer Research (2003), 63(21), 7221-7231
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Overexpression of the receptor tyrosine kinase HER-2/neu is associated with poor prognosis in patients with breast and ovarian cancer. Recent excitement has surrounded the therapeutic effects of HER-2-blocking therapy strategies and has rekindled interest on the mol. mechanisms of HER-2/neu in tumor biol. To study the role of HER-2/neu overexpression in vivo, the authors used a murine fibroblast cell line (NIH3T3-her2) conditionally expressing human HER-2/neu under control of a tetracycline-responsive promoter. Expression of HER-2 could be down-regulated below detection limit (>625-fold dilution) by exposure of NIH3T3-her2 cells to anhydrotetracycline (ATc). S.c. injection of NIH3T3-her2 cells into nude mice resulted in rapid tumor growth. Mice with mean tumor vols. of 0.2, 0.8, 1.9, and 14.9 cm3 were treated daily with 10 mg/kg ATc to switch off HER-2/neu expression, producing redns. in tumor size of 100, 98.1, 81.4, and 74.2%, resp., by 7 days after onset of ATc administration. Different long-term effects of HER-2 down-regulation were observed when mice with small (0.2 cm3), intermediate (0.8-1.2 cm3) and large (≥1.9 cm3) tumors received ATc for up to 40 days. Complete remission was observed for 100, 40, and 18% of the small-, intermediate-, and large-sized tumors, resp. However, after 20-45 days of ATc administration, recurrent tumor growth was observed for all mice, even in those with previous complete remissions. The time periods for which mean tumor volume could be suppressed to vols. <0.1 cm3 under ATc administration were 34, 22, 8, and 0 days for tumors with initial vols. of 0.2, 0.8, 1.9 and 14.9 cm3, resp. Interestingly, HER-2 remained below the detection limit in recurrent tumor tissue, suggesting that initially HER-2-dependent tumors switched to HER-2 independence. The "second hits" leading to HER-2-independent tumor growth have not yet been identified. The rapid regression of tumors after down-regulation of HER-2 was explained by two independent mechanisms: (a) a block in cell cycle progression, as evidenced by a decrease in Ki-67 antigen expression from 40% before ATc treatment to 8.3% after 7 days of ATc treatment; and (b) induction of apoptosis as demonstrated by caspase-3 activation and by the terminal deoxynucleotidyltransferase (Tdt)-mediated nick end labeling assay (TUNEL). In conclusion, the authors have shown that switching off HER-2

may disturb the sensitive balance between cell proliferation and cell death, leading to apoptosis and tumor remission. Tumor remission was dependent on the volume of the tumors before down-regulation of HER-2/neu.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:202649 HCAPLUS
DOCUMENT NUMBER: 138:238205
TITLE: Preparation of fused indoles as anticancer drugs.
INVENTOR(S): Weinberger, Heinz; Beckers, Thomas; Schmidt, Mathias; **Baasner, Silke**; Nickel, Bernd
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003020731 | A1 | 20030313 | WO 2002-EP9539 | 20020827 |
| W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR | | | | |
| DE 10143079 | A1 | 20030515 | DE 2001-10143079 | 20010903 |
| CA 2458399 | AA | 20030313 | CA 2002-2458399 | 20020827 |
| EP 1423393 | A1 | 20040602 | EP 2002-767436 | 20020827 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002012300 | A | 20041013 | BR 2002-12300 | 20020827 |
| CN 1551885 | A | 20041201 | CN 2002-817263 | 20020827 |
| NZ 531642 | A | 20050128 | NZ 2002-531642 | 20020827 |
| JP 2005508898 | T2 | 20050407 | JP 2003-525001 | 20020827 |
| ZA 2004001290 | A | 20040323 | ZA 2004-1290 | 20040218 |
| NO 2004000831 | A | 20040413 | NO 2004-831 | 20040225 |

PRIORITY APPLN. INFO.: DE 2001-10143079 A 20010903
WO 2002-EP9539 W 20020827

OTHER SOURCE(S): MARPAT 138:238205
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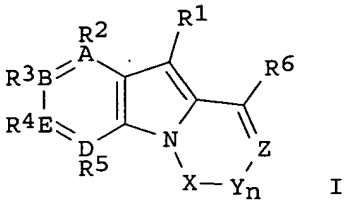


I

AB Title compds. [I; R1 = H, (substituted) aryl, heteroaryl, cycloalkyl, alkyl; A, B, D, E = C, N; R2-R5 = electron pair, H, halo, cyano, NO2, OH, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylcarbonyloxy, alkylsulfonyl, CO2H, amino, etc.; R6, R7, R8 = (substituted) aryl, heteroaryl, cycloalkyl, alkyl; X = CO, SO, SO2; Y = O, NR7; n = 0, 1; Z = CR8], were

prepared Thus, reaction of (5-methoxy-1H-indol-2-yl) Ph methanone oxime (preparation given) with carbonyldiimidazole in refluxing THF gave 5-methoxy-3-phenyl-1,2,5-oxadiazino[4,5-a]indol-6-one. This at 3.16 μg/mL showed 90.7% antiproliferative activity against HeLa/KB in an XTT cytotoxicity test.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:80889 HCAPLUS
DOCUMENT NUMBER: 136:272658
TITLE: Bis(1H-2-indolyl)methanones as a Novel Class of Inhibitors of the Platelet-Derived Growth Factor Receptor Kinase
AUTHOR(S): Mahboobi, Siavosh; Teller, Steffen; Pongratz, Herwig; Hufsky, Harald; Sellmer, Andreas; Botzki, Alexander; Uecker, Andrea; Beckers, Thomas; **Baasner, Silke**; Schaechtele, Christoph; Ueberall, Florian; Kassack, Matthias U.; Dove, Stefan; Boehmer, Frank-D.
CORPORATE SOURCE: Faculty of Chemistry and Pharmacy, Institute of Pharmacy, University of Regensburg, Regensburg, D-93040, Germany
SOURCE: Journal of Medicinal Chemistry (2002), 45(5), 1002-1018
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:272658

AB The novel lead bis(1H-2-indolyl)methanone inhibits autophosphorylation of platelet-derived growth factor (PDGF) receptor tyrosine kinase in intact cells. Various substituents in the 5- or 6-position of one indole ring increase or preserve potency, whereas most modifications of the ring structures and of the methanone group as well as substitution at both indoles result in weak or no activity. An ATP binding site model, derived by homol. from the FGFR-1 tyrosine kinase crystal structure suggesting hydrogen bonds of one indole NH and the methanone oxygen with the backbone carbonyl and amide, resp., of Cys684, explains why only one indole moiety is open for substitution and locates groups in the 5- or 6-position outside the pocket. Some of the most active derivs., inhibit both isoforms of the PDGF receptor kinase in intact cells, with IC50 of 0.1-0.3 μM, and purified PDGFβ-receptor in vitro, with IC50 of 0.09, 0.1, or 0.02 μM, resp. PDGF-stimulated DNA synthesis is inhibited by these derivs. with IC50 values of 1-3 μM. Kinetic anal. of one compound showed an ATP-competitive mode of inhibition. The compds. are inactive or weakly active toward a number of other tyrosine kinases, including the FGF receptor 1, EGF receptor, and c-Src kinase, as well as toward serine-threonine kinases, including different PKC isoforms and GRK2, and appear therefore selective for PDGF receptor inhibition.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:836852 HCAPLUS
DOCUMENT NUMBER: 136:112229
TITLE: Synthetic 2-Aroylindole Derivatives as a New Class of Potent Tubulin-Inhibitory, Antimitotic Agents
AUTHOR(S): Mahboobi, Siavosh; Pongratz, Herwig; Hufsky, Harald; Hockemeyer, Joerg; Frieser, Markus; Lyssenko, Alexei; Paper, Dietrich H.; Buergermeister, Jutta; Boehmer,

Frank-D.; Fiebig, Heinz-Herbert; Burger, Angelika M.; **Baasner, Silke**; Beckers, Thomas

CORPORATE SOURCE: Faculty of Chemistry and Pharmacy Institute of Pharmacy, University of Regensburg, Regensburg, D-93040, Germany

SOURCE: Journal of Medicinal Chemistry (2001), 44(26), 4535-4553
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:112229

AB A new class of simple synthetic antimitotic compds. based on 2-aroylindoles was discovered. (5-Methoxy-1H-2-indolyl)-phenylmethanone (I) as well as analogous 3-fluorophenyl- and 3-methoxyphenyl derivs. displayed high cytotoxicity of IC50 = 20 to 75 nM against the human HeLa/KB cervical, SK-OV-3 ovarian, and U373 astrocytoma carcinoma cell lines. The inhibition of proliferation correlated with the arrest in the G2/M phase of the cell cycle. In in vitro assays with tubulin isolated from bovine brain, in general antiproliferative activity correlated with inhibition of tubulin polymerization Thus, the antimitotic activity of 2-aroylindoles is explained by interference with the mitotic spindle apparatus and destabilization of microtubules. In contrast to colchicine, vincristine, nocodazole, or taxol, I did not significantly affect the GTPase activity of β-tubulin. Interestingly, selected compds. inhibited angiogenesis in the chorioallantoic membrane (CAM) assay. In xenograft expts., I was highly active after oral administration at 200 mg/kg against the human amelanocytic melanoma MEXF 989 in athymic nude mice. We conclude, that 2-aroylindoles constitute an interesting new class of antitubulin agents with the potential to be clin. developed for cancer treatment.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:816437 HCAPLUS

DOCUMENT NUMBER: 135:352771

TITLE: (Hetero)indole derivatives, their preparation, pharmaceutical compositions, and their use as antitumor agents

INVENTOR(S): Beckers, Thomas; **Baasner, Silke**; Klenner, Thomas; Mahboobi, Siavosh; Pongratz, Herwig; Frieser, Markus; Hufsky, Harald; Hockemeyer, Jorg; Fiebig, Heinz-Herbert; Burger, Angelika; Bohmer, Frank-D.

PATENT ASSIGNEE(S): Asta Medica A.-G., Germany

SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001082909 | A2 | 20011108 | WO 2001-EP4783 | 20010427 |
| WO 2001082909 | A3 | 20020314 | | |

W: AT, AU, BG, BR, BY, CA, CH, CN, CO, CZ, DE, DK, DZ, EE, ES, FI, GB, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, MD, TJ, TM

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

| | | | | | |
|---|---|---|---|---|---|
| DE 10020852 | A1 | 20011031 | DE 2000-10020852 | | 20000428 |
| DE 10102629 | A1 | 20020725 | DE 2001-10102629 | | 20010120 |
| CA 2407677 | AA | 20021028 | CA 2001-2407677 | | 20010427 |
| EP 1276720 | A2 | 20030122 | EP 2001-947247 | | 20010427 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR

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|---|---|---|---|---|---|
| BR 2001010414 | A | 20030211 | BR 2001-10414 | | 20010427 |
| JP 2004501092 | T2 | 20040115 | JP 2001-579784 | | 20010427 |
| EE 200200607 | A | 20040415 | EE 2002-607 | | 20010427 |
| AU 783459 | B2 | 20051027 | AU 2001-68984 | | 20010427 |
| NO 2002005150 | A | 20021216 | NO 2002-5150 | | 20021025 |
| BG 107309 | A | 20030930 | BG 2002-107309 | | 20021125 |
| PRIORITY APPLN. INFO.: | | | DE 2000-10020852 | A | 20000428 |
| | | | DE 2001-10102629 | A | 20010120 |
| | | | WO 2001-EP4783 | W | 20010427 |

OTHER SOURCE(S): CASREACT 135:352771; MARPAT 135:352771

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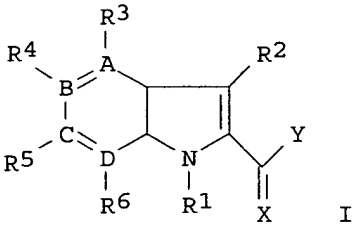

I

AB The invention discloses indole and heteroindole derivs. I [R1 = H, C1-6 alkyl, C1-6 alkylcarbonyl, etc.; R2 = H, halo, cyano, etc.; R3-R6 = H, halo, nitro, etc.; A-D = C, N; Y = (un)substituted C6-14 aryl, etc.; X = O, S, NH, CHOH], and tautomers, stereoisomers, mixts. and salts thereof, as well as the production thereof and the use thereof for the treatment of tumors.

L20 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:795073 HCAPLUS

DOCUMENT NUMBER: 135:331343

TITLE: Preparation of 1H-indol-2-yl aryl ketones and related compounds as antitumor agents

INVENTOR(S): Beckers, Thomas; **Baasner, Silke**; Klenner, Thomas; Mahboobi, Siavosh; Pongratz, Herwig; Frieser, Markus; Hufsky, Harald; Hockemeyer, Joerg; Fiebig, Heinz-Herbert; Burger, Angelika; Boehmer, Frank-D.

PATENT ASSIGNEE(S): Asta Medica A.-G., Germany

SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10020852 | A1 | 20011031 | DE 2000-10020852 | 20000428 |
| WO 2001082909 | A2 | 20011108 | WO 2001-EP4783 | 20010427 |

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| WO 2001082909 | | A3 | 20020314 | | | |
| W: AT, AU, BG, BR, BY, CA, CH, CN, CO, CZ, DE, DK, DZ, EE, ES, FI, GB, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, MD, TJ, TM | | | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | | | |
| US 2002091124 | | A1 | 20020711 | US 2001-843139 | | 20010427 |
| CA 2407677 | | AA | 20021028 | CA 2001-2407677 | | 20010427 |
| EP 1276720 | | A2 | 20030122 | EP 2001-947247 | | 20010427 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR | | | | | | |
| BR 2001010414 | | A | 20030211 | BR 2001-10414 | | 20010427 |
| JP 2004501092 | | T2 | 20040115 | JP 2001-579784 | | 20010427 |
| EE 200200607 | | A | 20040415 | EE 2002-607 | | 20010427 |
| US 2003158216 | | A1 | 20030821 | US 2002-279123 | | 20021024 |
| US 2003158216 | | A1 | 20030821 | US 2002-279123 | | 20021024 |
| NO 2002005150 | | A | 20021216 | NO 2002-5150 | | 20021025 |
| ZA 2002009137 | | A | 20040618 | ZA 2002-9137 | | 20021111 |
| BG 107309 | | A | 20030930 | BG 2002-107309 | | 20021125 |
| PRIORITY APPLN. INFO.: | | | | DE 2000-10020852 | A | 20000428 |
| | | | | DE 2001-10102629 | A | 20010120 |
| | | | | US 2001-843139 | B1 | 20010427 |
| | | | | WO 2001-EP4783 | W | 20010427 |

OTHER SOURCE(S): MARPAT 135:331343

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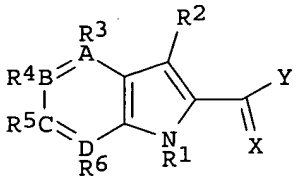


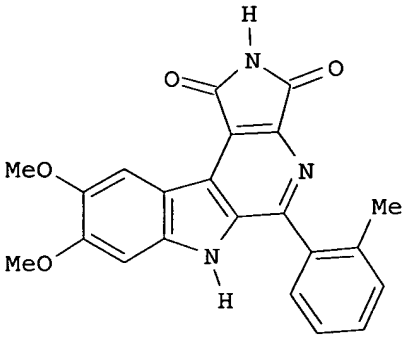

I

AB Use of title compds. [I; R1 = H, alkylcarbonyl, alkylaminoalkyl, dialkylaminoalkyl, (hetero)cyclyl; R2 = H, halo, cyano, NO2, (substituted) alkyl, alkoxy, etc.; A-D = N, (substituted) C; R3-R6 = free electron pair if A-D = N, or H, halo, cyano, NO2, alkyl, etc. if A-D = C; Y = (substituted) aryl; X = O, S, NH, (H,OH)], for preparation of drugs for treatment of tumor illness in mammals is claimed. Thus, 5-methoxy-1H-indol-2-yl Ph ketone (general preparation given) showed antitumor activity with IC50 = 96.5 nM in rat glioma cell lines C6.

L20 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2000:398021 HCAPLUS |
| DOCUMENT NUMBER: | 133:164199 |
| TITLE: | Pyrrolo[3,4-c]-β-carboline-diones as a novel class of inhibitors of the platelet-derived growth factor receptor kinase |
| AUTHOR(S): | Teller, Steffen; Eluwa, Stella; Koller, Markus; Uecker, Andrea; Beckers, Thomas; **Baasner, Silke**; Bohmer, Frank-D.; Mahboobi, Siavosh |
| CORPORATE SOURCE: | Research Unit Molecular Cell Biology, Medical Faculty, Friedrich Schiller University, Jena, D-07747, Germany |
| SOURCE: | European Journal of Medicinal Chemistry (2000), 35(4), 413-427 |

CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Members of the structurally diverse family of β-carbolines have previously been shown to exhibit a wide range of biol. activities. A novel synthetic strategy for generation of β-carbolines was developed, allowing imido-β-carbolines to be created in three steps from known compds. The compds. were screened for inhibition of platelet-derived growth factor (PDGF)-stimulated tyrosine phosphorylation in Swiss 3T3 fibroblasts. A number of the newly synthesized β-carbolines with moderate to potent inhibitory activity were revealed. β-Carboline I was found to be the most active derivative inhibiting purified PDGF receptor kinase and PDGF-receptor autophosphorylation in intact cells with IC50 values of 0.4 and 2.6 μM, resp. I also inhibited PDGF-stimulated DNA synthesis in Swiss 3T3 fibroblasts with an IC50 of 3.2 μM. The compound had no effect on Src or epidermal growth factor (EGF) receptor kinase activity and a six-seven-fold higher IC50 for inhibition of basic fibroblast growth factor (bFGF)-stimulated tyrosine phosphorylation or Kit/stem cell factor (SCF) receptor autophosphorylation, indicating a reasonable extent of kinase specificity. Thus, β-carbolines present a new lead of tyrosine kinase inhibitors with the capacity to selectively interfere with PDGF receptor signal transduction and PDGF-dependent cell growth.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:242550 HCAPLUS
DOCUMENT NUMBER: 133:236049
TITLE: A refined model for monitoring orthotropic tumor growth in nude mice
AUTHOR(S): Klenner, T.; Beckers, T.; Westhof, A.; **Baasner, S.**; Hilgard, P.
CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt/Main, Germany
SOURCE: Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 101-108
CODEN: COONEV; ISSN: 0250-3220
PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Athymic nude mice are commonly used in cancer research as hosts for xenografts of human tumors or oncogene-transformed recombinant cell lines. Tumorigenesis induced by the receptor tyrosine kinase HER2 was studied in vivo using the tTA/tetO7 system to allow conditional HER2 overexpression in NIH 3T3 fibroblasts. The tetoff system allows for a differential control of gene expression which is switched off by increasing concns. of tetracyclines. Because the expression of HER2 is related to the marker gene human secreted placental-type alkaline phosphatase (SEAP), tumor cell growth can be monitored in vitro and in vivo by simply measuring SEAP in culture supernatants or animal serum. Thus, a target-specific xenograft model was developed. However, it might be possible to use SEAP in other cell lines. Hence, the surgical methods were combined with the mol. biol. methods. SEAP was employed as a reporter gene for transfection of human tumor cell lines to develop a more sensitive, reliable and generally applicable method for monitoring tumor growth in nude mice independent of the location of the tumor.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:351174 HCAPLUS
DOCUMENT NUMBER: 126:312250
TITLE: Tumor cell lines using the human placenta-specific alkaline phosphatase gene as a reporter in the screening of antitumor-compositions
INVENTOR(S): Beckers, Thomas; Klenner, Thomas; **Baasner, Silke**
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany; Zentaris GmbH; Asta Medica Oncology GmbH & Co.
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 773293 | A2 | 19970514 | EP 1996-117448 | 19961030 |
| EP 773293 | A3 | 19981230 | | |
| EP 773293 | B1 | 20031203 | | |
| R: CH, DE, FR, GB, LI | | | | |
| DE 19542051 | A1 | 19970515 | DE 1995-19542051 | 19951110 |
| DE 19542051 | C2 | 20000323 | | |
| US 5837462 | A | 19981117 | US 1996-746383 | 19961108 |
| JP 09131184 | A2 | 19970520 | JP 1996-312624 | 19961111 |
| PRIORITY APPLN. INFO.: | | | DE 1995-19542051 A | 19951110 |

AB Tumor cell lines carrying an expression cassette for the secreted human placental alkaline phosphatase (SEAP) are described for use in the screening of compds. for their effectiveness as antitumor compds. These cells can be used for implantation into a test animal or in culture. Serum levels of the enzyme are proportional to the number of cells in the animal and can be used to measure rates of tumor growth before the tumor forms a palpable mass. Dicistronic expression constructs are used. The constructs use a constitutive or inducible promoter to drive expression of a gene that can induce tumorigenic growth of cells, e.g. erb2/HER2, an IRES, and the gene for SEAP with the two genes in any oder. The development of an in vivo system using the c-erbB2 gene in a dicistronic construct with the SEAP

gene is described. A constitutive expression cassette using the SV40 immediate-early promoter and an inducible cassette using a tetracycline-responsive operator are described.

L20 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:612409 HCAPLUS
DOCUMENT NUMBER: 125:272260
TITLE: Reversible tumorigenesis in mice by conditional expression of the HER2/c-erbB2 receptor tyrosine kinase
AUTHOR(S): **Baasner, Silke**; von Melchner, Harald; Klenner, Thomas; Hilgard, Peter; Beckers, Thomas
CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt/Main, 60314, Germany
SOURCE: Oncogene (1996), 13(5), 901-911
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study we describe the reversible transformation of NIH3T3 fibroblasts by overexpression of the HER2/c-erbB2 receptor tyrosine kinase. Cell lines expressing HER2 under control of a tetracycline-responsive promotor were isolated. Induction of HER2 expression resulted in cellular transformation in vitro as depicted by growth in soft agar and focus formation in tissue culture. Subsequent treatment of these cells with the effector anhydrotetracylin switched-off HER2 expression and induced morphol. and functional changes characteristic for non-transformed cells. S.c. transplantation of cells in nude mice resulted in the formation of solid tumors. Interestingly tumor formation was completely suppressed by treatment of the animals with anhydrotetracyline. Our findings indicate that overexpression of HER2 induces the transformed phenotype of NIH3T3 cells and is required for tumor formation and progression in nude mice. By linking the expression of the marker gene secreted placental alkaline phosphatase to the expression of HER2, a sensitive monitoring of tumor development in nude mice was feasible.

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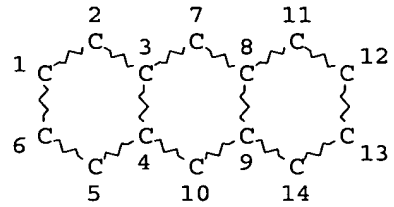


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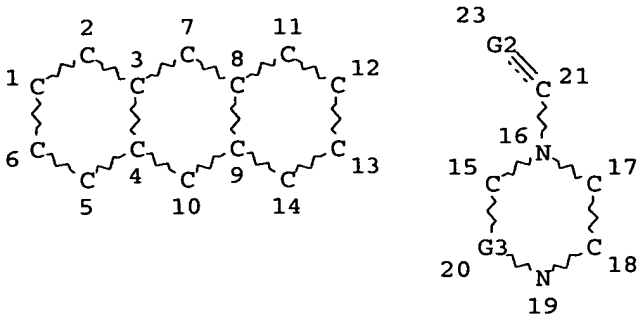

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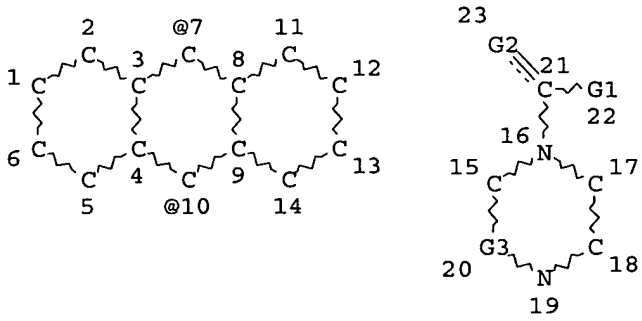

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NUMBER OF NODES IS 23

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L17 67 SEA FILE=HCAPLUS ABB=ON PLU=ON ("GUNTHER E"/AU OR "GUNTHER ECKHARD"/AU) NOT (L12 OR L16)
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L19 41 SEA FILE=HCAPLUS ABB=ON PLU=ON (("POLYMEROPOULOS E"/AU OR "POLYMEROPOULOS E E"/AU OR "POLYMEROPOULOS EMANUELE E"/AU OR "POLYMEROPOULOS EMMANUEL"/AU OR "POLYMEROPOULOS EMMANUEL E"/AU)) NOT (L12 OR L16 OR L17 OR L18)
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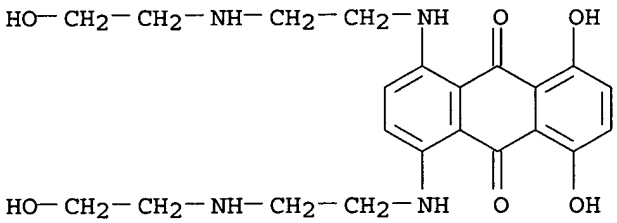
L23 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:587287 HCAPLUS
DOCUMENT NUMBER: 131:266704
TITLE: Anticancer drug sensitivity and expression of multidrug resistance markers in early passage human sarcomas
AUTHOR(S): Hoffmann, Jens; **Schmidt-Peter, Peter**; Hansch, Wolfgang; Naundorf, Helga; Bunge, Andreas; Becker, Michael; Fichtner, Iduna
CORPORATE SOURCE: Max-Delbruck-Center of Molecular Medicine, Berlin, 13122, Germany
SOURCE: Clinical Cancer Research (1999), 5(8), 2198-2204
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have established new human sarcoma lines and examined their sensitivity to common antitumor drugs and expression of putative multidrug resistance (MDR) proteins. Eighty-two sarcoma samples were transplanted in nude mice. Fourteen of these sarcomas were established as tumor cell lines. We determined a chemosensitivity profile to antitumor drugs (MDR drugs = doxorubicin, mitoxantrone, and vincristine; non-MDR drugs = cisplatin, ifosfamide, and bleomycin) for each tumor line in vivo. Response to chemotherapy with doxorubicin and ifosfamide was observed in 30-50% of these tumor lines. Our results obtained with xenotransplants are similar to the results documented in clin. trials in which doxorubicin and ifosfamide are effective in 30-50% of the patients. Furthermore, we examined expression of MDR-relevant markers like P-glycoprotein, MDR-associated protein, lung resistance protein, and mdr1 mRNA in these xenotransplants. A relationship between mdr1 mRNA expression and response to doxorubicin was demonstrated in >90% of our tumor lines. In six sarcomas with mdr1 mRNA expression, five were resistant against doxorubicin and cross-resistant

against several other drugs, whereas from eight sarcomas, which lacked detectable mdr1 mRNA, seven were sensitive to doxorubicin and other drugs. We found lung resistance protein or MDR-associated protein expressed in three resistant and mdr1 mRNA-pos. sarcomas. These results demonstrate that mdr1 mRNA expression is a putative marker for drug resistance in our sarcoma lines. We conclude, therefore, that inherent P-glycoprotein expression might be also responsible for drug resistance occurring in treatment of patients with sarcomas. The established tumor lines are useful for addnl. investigations on mechanisms of drug resistance in sarcomas and as models for preclin. screening of new antitumor drugs.

IT **65271-80-9**, Mitoxantrone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer drug sensitivity and expression of multidrug resistance markers in early passage human sarcomas)

RN 65271-80-9 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:618071 HCAPLUS

DOCUMENT NUMBER: 113:218071

TITLE: Development of a suspension-emulsion system for parenteral application in animals

AUTHOR(S): **Schmidt, Peter C.**; Perschbacher, Harald; Steffens, Klaus Juergen; Kraemer, Hans P.

CORPORATE SOURCE: Dep. Pharm. Technol., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.

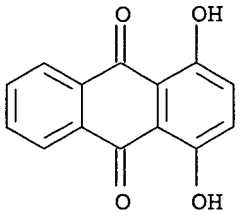
SOURCE: Acta Pharmaceutica Technologica (1989), 35(1), 34-7
CODEN: APTEDD; ISSN: 0340-3157

DOCUMENT TYPE: Journal

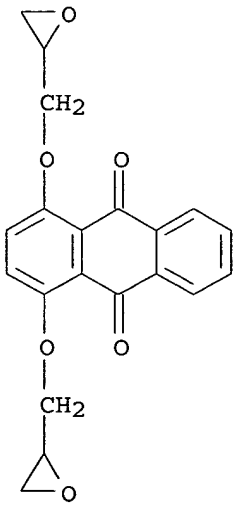
LANGUAGE: English

AB The pharmacol. activities of a new suspension-emulsion formulation of 2 antineoplastic drugs and spironolactone, all 3 only very slightly soluble in water and oils, were tested in mice and rats. The active ingredients were ground in medium chain triglycerides using a wet ball milling process. The resulting suspension was incorporated in an oil-water emulsion using lecithin and cholesterol as emulsifiers and then homogenized by a high-pressure homogenization process. The particle size of this suspension-emulsion system was in the range of 1 to 2 μm with a few particles up to 7 μm. In vivo results showed an increased bioavailability of the antineoplastic drugs when compared with an aqueous suspension. Spironolactone was more effective after i.p. administration than after i.v. application, but did not reach the effect of K canrenoate. The formulations were all well tolerated by the animals.

IT **81-64-1**, 1,4-Dihydroxyanthraquinone **98298-55-6**, S 830544
RL: BIOL (Biological study)
(suspension-emulsion parenteral system containing, development and bioavailability of)
RN 81-64-1 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy- (9CI) (CA INDEX NAME)



RN 98298-55-6 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



L23 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:445270 HCAPLUS
DOCUMENT NUMBER: 111:45270
TITLE: Pharmaceutical emulsions containing an oily phase, lecithin, an electrolyte and solid active agents
INVENTOR(S): List, Paul Heinz; **Schmidt, Peter Christian**; Steffens, Klaus Juergen; Perschbacher, Harald; Kraemer, Hans Peter; Sedlacek, Hans Harald
PATENT ASSIGNEE(S): Behringwerke A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
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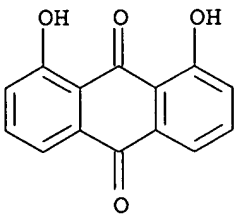
| DE 3623376 | A1 | 19880121 | DE 1986-3623376 | 19860711 |
| EP 256285 | A1 | 19880224 | EP 1987-109765 | 19870707 |
| EP 256285 | B1 | 19910320 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| AT 61730 | E | 19910415 | AT 1987-109765 | 19870707 |
| ES 2039214 | T3 | 19930916 | ES 1987-109765 | 19870707 |
| FI 8703044 | A | 19880112 | FI 1987-3044 | 19870709 |
| US 4801455 | A | 19890131 | US 1987-71382 | 19870709 |
| DK 8703597 | A | 19880112 | DK 1987-3597 | 19870710 |
| AU 8775536 | A1 | 19880114 | AU 1987-75536 | 19870710 |
| AU 597688 | B2 | 19900607 | | |
| JP 63023811 | A2 | 19880201 | JP 1987-171323 | 19870710 |
| ZA 8705044 | A | 19880224 | ZA 1987-5044 | 19870710 |
| CA 1302257 | A1 | 19920602 | CA 1987-541803 | 19870710 |
| PRIORITY APPLN. INFO.: | | | DE 1986-3623376 A | 19860711 |
| | | | EP 1987-109765 A | 19870707 |

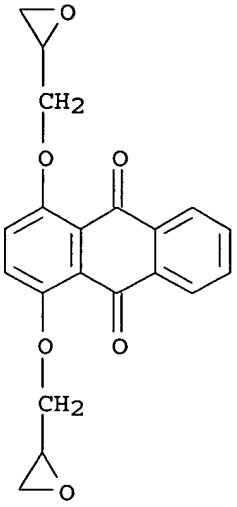
AB The title composition is suitable for the parenteral formulation of difficult to solubilize active agents; it contains a solid/liquid/liquid disperse system with particle size ≤5 μm which is obtained by emulsifying a ground substance with particle size ≤3 μm 1.5, an oily phase 8-30, an emulsifier 1.0-45, and H2O 64-90% by weight This emulsion is adjusted to isotonic conditions and homogenized in a high-pressure homogenizer. A 10% suspension of danthron (I) in Miglyol 812 (II) was ground to a particle size <3 μm; this was diluted 1-fold with II , and then was diluted with 24% lecithin in II, and this was mixed with cholesterol, H2O, and finally with NaCl, and finally homogenized. The product (40 g) contained I 0.200, II 3.800, Epikuron 170 (lecithin) 0.480, cholesterol 0.048, and 0.9% NaCl 35.472 g. A formulation (40 g) containing S830544 (anthraquinone derivative) 0.0124, II 3.9876, Epikuron 170 0.48, cholesterol 0.048, and NaCl 35.472 g was administered daily (4.64 mg/kg) to mice inoculated with 106 L1210 leukemia cells; the ratio of median survival time vs. an untreated control (MT/C) was 125%, whereas for mice treated with S830544 (200 mg/kg) in a tenside-containing medium the MT/C was 100%.

IT **117-10-2 98298-55-6**, S 830544
RL: BIOL (Biological study)
(pharmaceutical parenteral emulsion containing)

RN 117-10-2 HCAPLUS
CN 9,10-Anthracenedione, 1,8-dihydroxy- (9CI) (CA INDEX NAME)



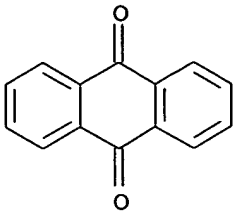

RN 98298-55-6 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



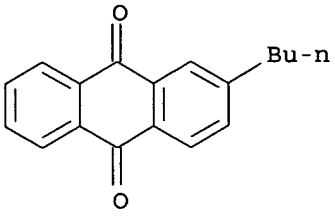
L23 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:534786 HCAPLUS
DOCUMENT NUMBER: 107:134786
TITLE: The action of anthraquinone sensitizers in the photo-oxidative degradation of low density polyethylene: mechanical evidence of dark processes
AUTHOR(S): Raab, M.; Hnat, V.; **Schmidt, P.**; Kotulak, L.; Taimr, L.; Pospisil, J.
CORPORATE SOURCE: Inst. Macromol. Chem., Czech. Acad. Sci., Prague, 162 06, Czech.
SOURCE: Polymer Degradation and Stability (1987), 18(2), 123-34
CODEN: PDSTDW; ISSN: 0141-3910
DOCUMENT TYPE: Journal
LANGUAGE: English

AB LDPE films containing 3 quinoid sensitizers, anthraquinone (I), 2-butylanthraquinone (II), and 2-octanoyloxyanthraquinone (III), were exposed to the UV light of a fluorescent tube. The kinetics of the photooxidative degradation was monitored by measuring IR spectra and 3 mech. characteristics derived from stress-strain traces, viz. strain at break, Young's modulus, and yield stress. During the first stage of the process, the greater solubility of II and III in LDPE compared to I was clearly manifested in both the mech. and spectral data. The sensitizers were consumed at the very beginning of the exposure, but once the degradation started it continued at a higher rate around introduced or intrinsic centers. The increase of yield stress values after a long-term dark storage which followed the irradiation period was ascribed to a slow continuous crystallization of the degraded polymer. No dark storage effect was found with samples not previously exposed to UV light.

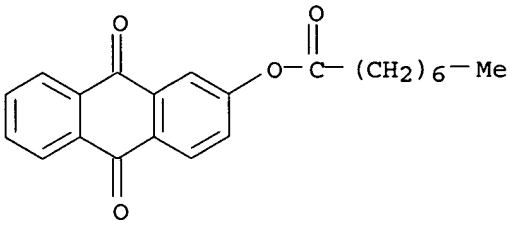
IT **84-65-1**, Anthraquinone **7504-51-0**, 2-Butylanthraquinone
**110484-84-9**
RL: USES (Uses)
(sensitizers, in photooxidative degradation of LDPE)
RN 84-65-1 HCAPLUS
CN 9,10-Anthracenedione (9CI) (CA INDEX NAME)



RN 7504-51-0 HCAPLUS
CN 9,10-Anthracenedione, 2-butyl- (9CI) (CA INDEX NAME)




RN 110484-84-9 HCAPLUS
CN Octanoic acid, 9,10-dihydro-9,10-dioxo-2-anthracenyl ester (9CI) (CA INDEX NAME)



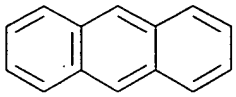

L23 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:111413 HCAPLUS
DOCUMENT NUMBER: 100:111413
TITLE: Optical absorption of molecules in the electric field of the double layer
AUTHOR(S): **Schmidt, P.**; Plieth, W.
CORPORATE SOURCE: Inst. Phys. Chem., Freie Univ., Berlin, D-1000/33, Fed. Rep. Ger.
SOURCE: Journal de Physique, Colloque (1983), (C10), 175-8
CODEN: JPQCAK; ISSN: 0449-1947
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structures and properties of organic monolayers adsorbed on a polished Pt electrode were studied with the help of modulation reflectance (MR) spectroscopy. The monolayers of p-aminonitrobenzene, p-(dimethylamino)nitrosobenzene, and p-(dimethylamino)nitrostilbene show electrochromic effects which allow the determination of the orientation of the adsorbed mols. and finally the calcn. of the double layer field strength. In addition to that, the MR spectrum of anthracene adsorbed on a Pt electrode

was also detected.

IT **120-12-7**, properties
RL: PRP (Properties)
(modulated reflectance spectra of, adsorbed on platinum electrode)

RN 120-12-7 HCAPLUS

CN Anthracene (8CI, 9CI) (CA INDEX NAME)



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